Health Science Reports

WILEY

Health Science Reports
Open Access

ORIGINAL RESEARCH OPEN ACCESS

Metabolic Outcomes of Changing From Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine to Rilpivirine/Tenofovir Alafenamide/Emtricitabine: A Longitudinal Study

Ping-Feng Wu[1,2,3] | Hsi-Hsun Lin[3,4] | Hsin-Pai Chen[1,2] | Po-Chieh Huang[1] | Meng-Yu Ke[1]

[1]Division of Infectious Diseases, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan | [2]School of Medicine, National Yang-Ming Chiao Tung University, Taipei, Taiwan | [3]Institute of Clinical Medicine, National Yang-Ming Chiao Tung University, Taipei, Taiwan | [4]Division of Infectious Diseases, E-Da Dachang Hospital, I-Shou University, Kaohsiung, Taiwan

Correspondence: Ping-Feng Wu (striefcloud@gmail.com)

Received: 2 April 2024 | **Revised:** 19 October 2024 | **Accepted:** 27 November 2024

Keywords: HIV | lipids | metabolic syndrome | tenofovir alafenamide | tenofovir disoproxil fumarate

ABSTRACT

Background and Aims: People living with human immunodeficiency virus (HIV, PLWH) are aging, and there are growing concerns regarding combined antiretroviral therapy (cART)-associated negative metabolic consequences. We aimed to investigate the metabolic outcomes of PLWH by replacing rilpivirine (RPV)/tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) with RPV/tenofovir alafenamide (TAF)/FTC.

Methods: This retrospective study enrolled PLWH who changed from RPV/TDF/FTC to RPV/TAF/FTC between January 2019 and September 2023. Metabolic profiles were compared 1 year before and 3 years after changing cART using Cochran's *Q* and one-way ANOVA. The independent risk factors for metabolic syndrome were analyzed using logistic regression.

Results: A total of 182 patients were enrolled. The prevalence of metabolic syndrome has increased from 28% to 40.7%. The prevalence of hypertension and abnormal lipid levels significantly increased in the first year after changing cART, but the prescription of medicine for dyslipidemia increased in the second year ($p = 0.025$) and that for hypertension increased in the third year ($p < 0.001$). In addition to the criteria, body mass index (BMI) before changing cART was the only predictor of metabolic syndrome in the third year (OR 1.36; 95% CI 1.19–1.55; $p < 0.001$). The prevalence of metabolic syndrome and BMI did not increase significantly during the second and third years.

Conclusions: A gradually higher prevalence of metabolic syndrome among PLWH occurred with changes from RPV/TDF/FTC to RPV/TAF/FTC but plateaued beyond 2 years. However, fewer drugs for dyslipidemia, diabetes, and hypertension were prescribed within the first year after changing cART.

1 | Introduction

With the introduction and advancement of combined antiretroviral therapy (cART), people living with human immunodeficiency virus (HIV, PLWH) have a nearly normal life expectancy, similar to that of the general population [1, 2]. There are growing concerns regarding the cART-associated negative metabolic consequences because these populations are aging. Metabolic syndrome includes clustering risk factors for abdominal obesity, hypertension,

hyperglycemia, and dyslipidemia, and is associated with cardiovascular diseases and diabetes [3]. A previous study showed that the prevalence of metabolic syndrome among global PLWH was as high as 16.7%–31.3% [4]. Another meta-analysis from Africa indicated that the prevalence of metabolic syndrome in PLWH was significantly higher than that in HIV-negative individuals (21.5% vs. 12.0%) [5]. However, most of the abovementioned meta-analyses were conducted in Western countries and Africa, and information on metabolic syndrome in PLWH in Asia is limited [6].

Tenofovir disoproxil fumarate (TDF) is a highly effective and common cART agent. Recently, TDF has been progressively superseded by tenofovir alafenamide (TAF) owing to its bone and renal toxicity [7–9]. In contrast, weight gain and increased dyslipidemia after switching from TDF to TAF have been reported in previous literature [10–14]. Among patients who switched from TDF to TAF, there were significant increases in body weight (+1.5–1.7 kg), total cholesterol (+15 mg/dL),
low-density lipoprotein cholesterol (LDL-C) (+6.6–9 mg/dL) and triglycerides (+12–18.9 mg/dL) during 18–24 months [11, 12, 14]. When comparing patients with continuing TDF, significant weight gain (+0.5 kg) and rising blood lipid, including total cholesterol (+7.9 mg/dL), LDL-C (+4.1 mg/dL), and triglycerides (+11.2 mg/dL) were shown in those with changing to TAF [10]. Nevertheless, body weight and body mass index (BMI) can not be distinguished from central obesity, and normal-weight central obesity is associated with a higher risk of mortality and poor metabolic consequences [15, 16]. Furthermore, information regarding metabolic syndrome in PLWH with changes from TDF to TAF is scarce.

To address the importance of different cART regimens on metabolic consequences, the aim of our study was to evaluate the development and associated risk factors of metabolic syndrome among PLWH with switching from rilpivirine (RPV)/TDF/emtricitabine (FTC) to RPV/TAF/FTC.

2 | Methods

2.1 | Study Design and Subjects

This retrospective observational study was conducted at a tertiary medical center in Taiwan. PLWH aged ≥ 20 years who received cART changing from RPV/TDF/FTC to RPV/TAF/FTC between January 2019 and December 2023 were included. No other changes in cART regimens were allowed during the study period. Patients with available information regarding BMI, serum HIV RNA level, $CD4^+$ cell counts, serum lipid levels, and variables of metabolic syndrome at least every 6 months before and after the change in cART were enrolled. Patients who received RPV/TDF/FTC less than 1 year before changing cART or those missing the abovementioned records were excluded. The index date was set as 1 year before changing the cART. The study population was followed up for 3 years after the change in cART. This study was approved by the Institutional Review Board of Taipei Veterans General Hospital, and written informed consent was obtained from all participants.

2.2 | Variables and Definitions

Information from the medical records of enrolled patients was reviewed by specialists in infectious diseases. The acquired variables were as follows: age at changing cART, sex, underlying condition, HIV transmission route, duration of HIV infection, serum HIV RNA level, $CD4^+$ cell counts, BMI, serum lipid levels, and records of metabolic syndrome. Serum HIV RNA levels were checked using cobas HIV-1 (Roche Diagnostics, Mannheim, Germany), and all undetectable HIV RNA levels (< 20 copies/mL) were set to 19 copies/mL for data consistency. The abovementioned data was measured over 6-month intervals (with a window period of ±14 days). Metabolic syndrome was defined as any three of the following factors: (1) elevated waist circumference (≥ 90 cm in males and ≥ 80 cm in females among Asians), (2) elevated triglycerides ≥ 150 mg/dL or any medicine for elevated triglycerides, (3) reduced high-density lipoprotein cholesterol (HDL-C, < 40 mg/dL in male and < 50 mg/dL in female), or any medicine for reduced HDL-C; (4) elevated blood pressure (systolic ≥ 130 and/or diastolic ≥ 85 mmHg) or anti-hypertensive drug use, and (5) elevated fasting glucose ≥ 100 mg/dL or any medicine for hyperglycemia [3].

The metabolic outcomes of the study population were assessed 1 year before and 1, 2, and 3 years after changing from RPV/TDF/FTC to RPV/TAF/FTC. The primary outcome was metabolic syndrome prevalence. Longitudinal changes in serum lipid levels, body weight and BMI were evaluated. Finally, risk factors for metabolic syndrome were investigated.

2.3 | Statistical Analysis

The variables of metabolism were analyzed using χ^2 or Fisher's exact tests for categorical data and the Student's *t*- or Mann–Whitney *U* test for continuous data. Data before and after changing cART were compared using Cochran's *Q* test and one-way analysis of variance (ANOVA). Two-tailed tests were used to determine statistical significance, and a value of $p < 0.05$ was considered significant. To identify the independent risk factors for metabolic syndrome after changing cART, logistic regression with univariate and multivariate analyses was utilized for the criteria of metabolic syndrome and other variables. All biologically plausible variables with values of $p < 0.20$ in the univariate testing were entered into the model. All statistical analyses were performed using SPSS software version 20 (SPSS INC, Chicago, IL, USA).

3 | Results

A total of 182 patients who changed cART from RPV/TDF/FTC to RPV/TAF/FTC were enrolled in our study. The mean age was 43.1 years, and 174 (95.6%) were male of whom 165 (94.8%) were transmitted by HIV through men who have sex with men (Table 1). The mean duration of HIV infection was 10.4 years (interquartile range 6–14 years). There were almost all of the study population receiving the change in cART under mean plasma HIV viral load below 50 copies/mL (173/182, 95.1%) and

TABLE 1 | Baseline clinical characteristics of PLWH at the change of cART from rilpivirine/tenofovir disoproxil fumarate/emtricitabine to rilpivirine/tenofovir alafenamide/emtricitabine.

Baseline characteristics	Number of patients (%)
Total patients	182 (100.0)
Age (years), median (IQR)	42 (35–49)
Male	174 (95.6)
Underlying conditions	
Diabetes mellitus	17 (9.3)
Dyslipidemia	111 (70.0)
Hypertension	82 (45.1)
HIV transmission route	
Men who have sex with men	165 (90.7)
Intravenous drug use	7 (3.8)
Heterosexual	10 (5.5)
Duration of HIV infection (years)	10 (6–14)
Serum HIV RNA levels (copies/mL), median (IQR)	19 (19–22)
$CD4^+$ cell counts (cells/μL), median (IQR)	607 (495–802)

Abbreviations: cART (combined antiretroviral therapy); HIV (human immunodeficiency virus); IQR (interquartile range); PLWH (people living with HIV).

mean $CD4^+$ cell count above 200 cells/μL (181/182, 99.5%). The most common underlying metabolic condition was dyslipidemia (111/182, 70.0%) at baseline.

The changes in metabolic profiles and associated medicines among 182 patients from 1 year before to 3 years after changing cART are shown in Table 2. The prevalence of dyslipidemia, including total cholesterol ≥ 200 mg/dL, LDL-C ≥ 130 mg/dL, HDL-C < 40 mg/dL in male or 50 mg/dL in female, and triglycerides ≥ 150 mg/dL, were significantly increased during the study period ($p < 0.001$), but the ratios of total cholesterol to HDL-C were not significantly different ($p = 0.612$). Of the criteria of metabolic syndrome, only the prevalence of fasting blood sugar ≥ 100 mg/dL was not statistically different ($p = 0.554$). The median body weight had been increased from 68 kg of 1 year before to 71.1 kg of 3 years after changing cART ($p < 0.001$), and the proportion of patients with BMI ≥ 23 had also been increased from 59.9% to 70.3% ($p < 0.001$). The number of patients who fulfilled the metabolic syndrome criteria increased from 28.0% 1 year before to 40.7% 3 years after changing cART ($p < 0.001$). Despite a significant increase in almost all metabolic profiles during the study period, there were no statistically significant differences in lipid levels, BMI, and hypertension after the first year of changing cART. Although the use of drugs for hypertension, diabetes, and dyslipidemia increased 1 year before and 3 years after changing cART, there was no significant increase during the first year after changing cART ($p = 1.000$).

We analyzed the influence of metabolic syndrome criteria 1 year before changing cART on the development of metabolic syndrome in the third year. In the multivariate logistic regression model, triglycerides ≥ 150 mg/dL (OR 4.18; 95% CI 1.76–9.94; $p = 0.001$), HDL-C < 40 mg/dL in male or 50 mg/dL in female (OR 2.84; 95% CI 1.38–5.86; $p = 0.005$) and prevalence of hypertension (OR 2.96; 95% CI 1.42–6.17; $p = 0.004$) were independent predictors. Table 3 demonstrates that different proportions of criteria among PLWH fulfilled the diagnosis of metabolic syndrome before and after changing cART. Among patients with metabolic syndrome, a noticeable increase in the criteria of waist circumference occurred from 27.5% to 71.6% during the study period, while there was no increase in the criteria for HDL-C from 80.4% to 77.0%. There was a high prevalence of hypertension and fasting blood sugar ≥ 100 mg/dL, but the uses of the drug were only increased from 23.5% to 24.3% for hypertension and from 15.7% to 16.2% for hyperglycemia.

Logistic regression analysis was used to further compare the influence of factors other than metabolic syndrome criteria before changing cART on the diagnosis of metabolic syndrome in the third year, which was shown as Table 4. Patients with older age ($p = 0.007$), longer duration of HIV infection ($p = 0.008$), and higher BMI before switch ($p < 0.001$) had a higher risk of metabolic syndrome in the univariate analysis. In the multivariate analysis, higher BMI was the only independent predictor (OR 1.36; 95% CI 1.19–1.55; $p < 0.001$). Total cholesterol ≥ 200 mg/dL and LDL-C ≥ 130 mg/dL had no significant effects on the development of metabolic syndrome.

4 | Discussion

Most PLWH can suppress HIV viremia and recover their serum $CD4^+$ cell counts under cART currently. Aging is an issue of growing concern among PLWH in the current era, and the negative metabolic consequences of cART are worth investigating. Our study indicated that the prevalence of metabolic syndrome among PLWH increased within 3 years after changing cART from RPV/TDF/FTC to RPV/TAF/FTC, and that BMI before changing cART was an independent predictor of metabolic syndrome in the third year. However, the prevalence of metabolic syndrome and BMI did not significantly increase during the second and third years after changing cART.

Previous studies have reported that an increase in serum lipid levels in PLWH who switched from TDF to TAF [10–12, 17–20]. A study in Italy demonstrated a significant increase in total cholesterol, HDL-C, LDL-C, and triglycerides after a median follow-up of 12 weeks (range, 8–24 weeks) from RPV/TDF/FTC to RPV/TAF/FTC [11]. Studies from the USA conducted by Schafer et al. [19] and Hagins et al. [18] showed similar results in 1 and 2 years after changing from TDF to TAF, respectively. Another study from Spain also reported higher levels of all serum lipid levels 3 years after changing from TDF to TAF [10]. Mallon et al. further described that there was a significant increase in LDL-C initially after the change from TDF to TAF, which then plateaued after 9 months [12]. Nevertheless, the replacement of TDF with TAF remains the main trend in the current cART. A more recent study showed similar results, but there was no significant weight change after switching from TAF-based regimens

TABLE 2 | Metabolic profiles and the use of drugs before and after changing cART from rilpivirine/tenofovir disoproxil fumarate/emtricitabine to rilpivirine/tenofovir alafenamide/emtricitabine.

	1 year before changing cART	1 year after changing cART	2 years after changing cART	3 years after changing cART	*p* value
Lipid profiles					
Total cholesterol ≥ 200 mg/dL	19 (10.4%)	45 (24.7%)	59 (32.4%)	65 (35.7%)	< 0.001
LDL-C ≥ 130 mg/dL	28 (15.4%)	50 (27.5%)	57 (31.3%)	61 (33.5%)	< 0.001
HDL-C < 40 or 50 mg/dL	86 (47.3%)	59 (32.4%)	51 (28.0%)	70 (38.5%)	< 0.001
Triglyceride ≥ 150 mg/dL	43 (23.6%)	71 (39.0%)	60 (33.0%)	69 (37.9%)	< 0.001
Total cholesterol-HDL-C ratio	4.1 (3.3–4.8)	3.9 (3.2–4.8)	4.0 (3.3–4.8)	4.1 (3.3–5.0)	0.612
Waist circumference ≥ 90 cm in male or 80 cm in female	27 (14.8%)	56 (30.8%)	74 (40.7%)	80 (44.0%)	< 0.001
Hypertension	82 (45.1%)	103 (56.6%)	112 (61.5%)	108 (59.3%)	< 0.001
Fasting blood sugar ≥ 100 mg/dL	66 (36.3%)	65 (35.7%)	72 (39.6%)	72 (40.0%)	0.554
Body weight (kg)	68 (61–77)	70.5 (63–78.3)	71.5 (64–80)	71.1 (63.2–80.2)	< 0.001
Body mass index ≥ 23	109 (59.9%)	121 (66.5%)	128 (70.3%)	128 (70.3%)	< 0.001
Drug for hypertension	15 (8.2%)	16 (8.8%)	20 (11.0%)	25 (13.7%)	< 0.001
Drug for diabetes mellitus	10 (5.5%)	10 (5.5%)	12 (6.6%)	16 (8.8%)	0.008
Drug for dyslipidemia	5 (2.7%)	9 (4.9%)	15 (8.2%)	26 (14.3%)	< 0.001
Metabolic syndrome	51 (28.0%)	67 (36.8%)	73 (40.1%)	74 (40.7%)	< 0.001

Abbreviations: cART (combined antiretroviral therapy); HDL-C (high-density lipoprotein cholesterol); LDL-C (low-density lipoprotein cholesterol).

to dolutegravir/lamivudine or long-acting cabotegravir/RPV, and no significant improvement in the lipid profile after switching from TAF-based regimens to long-acting cabotegravir/RPV [21]. These metabolic effects of switching are mostly attributed to the loss of the beneficial effects of TDF rather than the adverse effects of TAF. The abovementioned literature comes from Western countries, and information from Asia regarding the changes in the lipid profile with cART changing from TDF to TAF is limited [20]. In our study, the increase in lipid profiles was consistent with previous studies, and we further indicated that the increase in serum lipid levels was only significant in the first year after changing from RPV/TDF/FTC to RPV/TAF/FTC, and the increase progressive slowed during the second and third years.

Similar to the trend of increased serum lipid levels observed in our study, the prevalence of hypertension significantly increased in the first year after changing from RPV/TDF/FTC to RPV/TAF/FTC. However, the prescription of medication for dyslipidemia had significantly increased since the second year ($p = 0.025$), and that for hypertension had increased since the third year ($p < 0.001$). As there was a potential time lag between the cART switch, metabolic change, and observation of this change by the clinician, the delay of prescription for comorbidities could occur. This could explain that drugs for comorbidities were not added during the first year. A recent retrospective study indicated that pre-exposure prophylaxis for HIV infection with TAF use was associated with a higher risk of incident hypertension (OR 1.64; 95% CI 1.05–2.56) and statin initiation (OR 2.33; 95% CI 1.41–3.85), and larger risk difference of statin initiation was shown among individuals aged ≥ 40 years [22]. Kwarisiima et al. reported better hypertension control from 15% to 46% after an intervention in an integrated chronic disease clinic [23]. Rethy et al. raised concerns about inappropriate anti-hypertensive agents use among PLWH, which resulted in an increased risk of cardiovascular diseases [24]. These findings remind clinical physicians to closely monitor and prescribe medicines for developing hypertension and dyslipidemia, especially when changing from TDF to TAF in cART.

The prevalence of metabolic syndrome among PLWH varies regionally and has been reported to change from 24%–27% during 2000–2009 [25–28] to 23.6%–34% during 2013-2017 [29, 30]. A more recent study published in 2023 from Africa showed 30.7% PLWH fulfilled the criteria of metabolic syndrome [31]. The literature on metabolic syndrome in PLWH mostly comprises cross-sectional studies. Our study showed the longitudinally increased trend of metabolic syndrome (from 28.0% to 40.7%) after changing from RPV/TDF/FTC to RPV/TAF/FTC, especially during the period of initial 2 years. The most significant factor was an increase in waist circumference, from 27.5% to 71.6%, during the study period. Previous studies described that BMI was significantly associated with metabolic syndrome [25, 32]. We further indicated that BMI was the only independent predictor of metabolic syndrome after changing from RPV/TDF/FTC to RPV/TAF/FTC.

The present study has several limitations. First, clinical data were collected from a single tertiary hospital and patients in

TABLE 3 | Different proportions of criteria among PLWH fulfilled the diagnosis of metabolic syndrome before and after changing cART from rilpivirine/tenofovir disoproxil fumarate/emtricitabine to rilpivirine/tenofovir alafenamide/emtricitabine.

1 year before changing cART	1 year after changing cART	2 years after changing cART	3 years after changing cART
$n = 51$	$n = 67$	$n = 73$	$n = 74$
Waist circumference ≥ 90 cm in males or 80 cm in females			
14 (27.5%)	42 (62.7%)	57 (78.1%)	53 (71.6%)
Triglyceride ≥ 150 mg/dL			
31 (60.8%)	51 (76.1%)	47 (64.4%)	51 (68.9%)
HDL-C < 40 mg/dL in males or 50 mg/dL in females			
41 (80.4%)	43 (64.2%)	42 (57.5%)	57 (77.0%)
Hypertension			
44 (86.3%)	59 (88.1%)	66 (90.4%)	67 (90.5%)
Fasting blood sugar ≥ 100 mg/dL			
38 (74.5%)	46 (68.7%)	51 (69.9%)	53 (71.6%)
Drug for hypertension			
12 (23.5%)	11 (16.4%)	13 (17.8%)	18 (24.3%)
Drug for diabetes mellitus			
8 (15.7%)	6 (9.0%)	7 (9.6%)	12 (16.2%)
Drug for dyslipidemia			
5 (9.8%)	7 (10.4%)	6 (8.2%)	17 (23.0%)

Abbreviations: cART (combined antiretroviral therapy); HDL-C (high-density lipoprotein cholesterol); PLWH (people living with human immunodeficiency virus).

whom cART was switched from RPV/TDF/FTC to RPV/TAF/FTC were limited. A relatively small number of patients were included in this study. Second, 95.6% of the participants were male, and our findings may not be generalizable to female. Since females were reported as one of the etiologies of greater weight gain when switching from TDF to TAF [10], and females had more than double the odds of having metabolic syndrome than males [29], our results might underestimate the prevalence of poor metabolic outcomes in female patients. Based on information from the Taiwan Centers for Disease Control in December 2022, males comprised 94.9% of patients with HIV infection in Taiwan, which is similar to the findings of our study. Third, some pre-existing risk factors for metabolic syndrome, such as smoking, alcohol consumption, high-fat diet, stressful and sedentary lifestyles, and family history of diabetes mellitus, before the change of cART were not collected in this study. Fourth, we lacked a control group, including PLWH who did not switch cART, to evaluate the influence of time change on our results. Lastly, the time of blood collection for biochemical analysis was not controlled. In our hospital, PLWH undergo regular blood tests every 6 months to monitor their lipid profiles, and they receive thorough education about the importance of fasting before the examination. Fasting status was rechecked by a medical technologist at the blood draw counter to avoid any influence of meals on serum lipid results. Despite these limitations, this longitudinal retrospective cohort

TABLE 4 | Influence of baseline factors other than metabolic syndrome criteria on developing metabolic syndrome in the third year after changing cART from rilpivirine/tenofovir disoproxil fumarate/emtricitabine to rilpivirine/tenofovir alafenamide/emtricitabine.

Characteristics	Metabolic syndrome No. (%)	Non-metabolic syndrome No. (%)	Univariate analysis *p* value	Multivariate analysis Odds Ratio(95% CI)	Multivariate analysis *p* value
Age (years), median (IQR)	45 (39–52)	39 (33–48)	0.007	1.017 (0.978–1.057)	0.403
Male	69 (93.2)	105 (97.2)	0.198	0.692 (0.123–3.903)	0.677
Men who have sex with men	65 (87.8)	100 (92.6)	0.279		
Duration of HIV infection (years)	12 (6–16.25)	8.5 (6–12.75)	0.008	1.055 (0.989–1.125)	0.105
Serum HIV RNA levels (copies/mL), median (IQR)	19 (19–22.5)	19 (19–21.75)	0.240		
$CD4^+$ cell counts (cells/μL), median (IQR)	611.5 (537–820.75)	603 (463.75–764.5)	0.181	1.000 (0.999–1.002)	0.863
Total cholesterol ≥ 200 mg/dL	10 (13.5)	9 (8.3)	0.262		
LDL-C ≥ 130 mg/dL	15 (20.3)	13 (46.4)	0.130	1.390 (0.576–3.355)	0.463
Body mass index	25.27 (23.11–27.03)	22.76 20.86–24.60)	< 0.001	1.357 (1.192–1.546)	< 0.001

Abbreviations: cART (combined antiretroviral therapy); HIV (human immunodeficiency virus); IQR (interquartile range); LDL-C (low-density lipoprotein cholesterol).

study represents serial changes in serum lipid levels, body weight, and metabolic syndrome during the switch from RPV/TDF/FTC to RPV/TAF/FTC. We believe that the findings of our study may provide useful information regarding PLWH experiencing gradual aging in the current era.

In conclusion, we found a gradually higher prevalence of metabolic syndrome among PLWH with cART switched from RPV/TDF/FTC to RPV/TAF/FTC, which plateauing beyond 2 years. The BMI before changing cART was an independent predictor of metabolic syndrome. In addition, there were fewer prescriptions of medication for dyslipidemia and hypertension. Physicians should closely monitor the values of metabolic profiles among PLWH under cART, especially when changing from TDF to TAF.

Author Contributions

Ping-Feng Wu: conceptualization, writing–original draft. **Hsi-Hsun Lin:** conceptualization, investigation, writing–review and editing. **Hsin-Pai Chen:** investigation, writing–review and editing. **Po-Chieh Huang:** data curation, formal analysis. **Meng-Yu Ke:** data curation, formal analysis.

Acknowledgments

We thank Roy Chen-Chih Wu for his thoughtful comments and the Medical Science & Technology Building of Taipei Veterans General Hospital for providing the experimental space and facilities.

Ethics Statement

This study was approved by the Institution Review Board of Taipei Veterans General Hospital, and the written informed consent was obtained from all study participants.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The corresponding author had full access to all of the data in this study and took complete responsibility for the integrity of the data and accuracy of the data analysis. Data supporting the findings of this study are available from the corresponding author upon reasonable request.

Transparency Statement

The lead author Ping-Feng Wu affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

References

1. S. Teeraananchai, S. Kerr, J. Amin, K. Ruxrungtham, and M. Law, "Life Expectancy of HIV-Positive People After Starting Combination Antiretroviral Therapy: A Meta-Analysis," *HIV Medicine* 18, no. 4 (2017): 256–266.

2. Antiretroviral Therapy Cohort Collaboration. "Survival of HIV-Positive Patients Starting Antiretroviral Therapy Between 1996 and 2013: A Collaborative Analysis of Cohort Studies," *Lancet HIV* 4, no. 8 (2017): e349–e356.

3. K. G. Alberti, R. H. Eckel, S. M. Grundy, et al., "Harmonizing the Metabolic Syndrome: A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity," *Circulation* 120, no. 16 (2009): 1640–1645.

4. K. A. Nguyen, N. Peer, E. J. Mills, and A. P. Kengne, "A Meta-Analysis of the Metabolic Syndrome Prevalence in the Global HIV-Infected Population," *PLoS One* 11, no. 3 (2016): e0150970.

5. O. O. Todowede, S. Z. Mianda, and B. Sartorius, "Prevalence of Metabolic Syndrome Among HIV-Positive and HIV-Negative Populations in Sub-Saharan Africa—A Systematic Review and Meta-Analysis," *Systematic Reviews* 8, no. 1 (2019): 4.

6. W. M. Han, M. G. Law, J. Y. Choi, et al., "Weight Changes, Metabolic Syndrome and All-Cause Mortality Among Asian Adults Living With HIV," *HIV Medicine* 23, no. 3 (2022): 274–286.

7. R. D. Cooper, N. Wiebe, N. Smith, P. Keiser, S. Naicker, and M. Tonelli, "Systematic Review and Meta-Analysis: Renal Safety of Tenofovir Disoproxil Fumarate in HIV-Infected Patients," *Clinical Infectious Diseases* 51, no. 5 (2010): 496–505.

8. J. E. Gallant, E. S. Daar, F. Raffi, et al., "Efficacy and Safety of Tenofovir Alafenamide Versus Tenofovir Disoproxil Fumarate Given as Fixed-Dose Combinations Containing Emtricitabine as Backbones for Treatment of HIV-1 Infection in Virologically Suppressed Adults: A Randomised, Double-Blind, Active-Controlled Phase 3 Trial," *Lancet HIV* 3, no. 4 (2016): 158–165.

9. S. K. Gupta, F. A. Post, J. R. Arribas, et al., "Renal Safety of Tenofovir Alafenamide vs. Tenofovir Disoproxil Fumarate: A Pooled Analysis of 26 Clinical Trials," *AIDS* 33, no. 9 (2019): 1455–1465.

10. J. Martinez-Sanz, S. Serrano-Villar, A. Muriel, et al., "Metabolic-Related Outcomes After Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in Adults With HIV: A Multicenter Prospective Cohort Study," *Clinical Infectious Diseases* 76, no. 3 (2022): e652–e660.

11. L. Taramasso, A. Di Biagio, N. Riccardi, et al., "Lipid Profile Changings After Switching From Rilpivirine/Tenofovir Disoproxil Fumarate/Emtricitabine to Rilpivirine/Tenofovir Alafenamide/Emtricitabine: Different Effects in Patients With or Without Baseline Hypercholesterolemia," *PLoS One* 14, no. 10 (2019): e0223181.

12. P. W. G. Mallon, L. Brunet, J. S. Fusco, et al., "Lipid Changes After Switch From TDF to TAF in the OPERA Cohort: LDL Cholesterol and Triglycerides," *Open Forum Infectious Diseases* 9, no. 1 (2022): ofab621.

13. H. H. Chang, "Weight Gain and Metabolic Syndrome in Human Immunodeficiency Virus Patients," *Infection & Chemotherapy* 54, no. 2 (2022): 220–235.

14. B. Surial, C. Mugglin, A. Calmy, et al., "Weight and Metabolic Changes After Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in People Living With HIV: A Cohort Study," *Annals of Internal Medicine* 174, no. 6 (2021): 758–767.

15. A. G. Dulloo, J. Jacquet, G. Solinas, J. P. Montani, and Y. Schutz, "Body Composition Phenotypes in Pathways to Obesity and the Metabolic Syndrome," supplement, *International Journal of Obesity* 34, no. S2 (2010): S4–S17.

16. K. R. Sahakyan, V. K. Somers, J. P. Rodriguez-Escudero, et al., "Normal-Weight Central Obesity: Implications for Total and Cardiovascular Mortality," *Annals of Internal Medicine* 163, no. 11 (2015): 827–835.

17. J. Lagoutte-Renosi, M. Flammang, C. Chirouze, et al., "Real-Life Impact on Lipid Profile of a Switch From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide in HIV-Infected Patients," *Current HIV Research* 19, no. 1 (2021): 84–89.

18. D. Hagins, C. Orkin, E. Daar, et al., "Switching to Coformulated Rilpivirine (RPV), Emtricitabine (FTC) and Tenofovir Alafenamide From Either RPV, FTC and Tenofovir Disoproxil Fumarate (TDF) or

Efavirenz, FTC and TDF: 96-week Results From Two Randomized Clinical Trials," *HIV Medicine* 19, no. 10 (2018): 724–733.

19. J. J. Schafer, K. N. Sassa, J. R. O'Connor, A. Shimada, S. W. Keith, and J. A. DeSimone, "Changes in Body Mass Index and Atherosclerotic Disease Risk Score After Switching From Tenofovir Disoproxil Fumarate to Tenofovir Alafenamide," *Open Forum Infectious Diseases* 6, no. 10 (2019): ofz414.

20. Y. S. Huang, C. Y. Cheng, H. Y. Sun, et al., "Week 96 Results of Switching From Tenofovir Disoproxil Fumarate-Based Antiretroviral Therapy to Coformulated Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide Among HIV/Hepatitis B Virus-Coinfected Patients," *Microbiology Spectrum* 11, no. 3 (2023): e0512522.

21. J. Damas, A. Munting, J. Fellay, et al, "Weight, Anthropometric and Metabolic Changes After Discontinuing Antiretroviral Therapy Containing Tenofovir Alafenamide (TAF) in People With HIV," *Clinical Infectious Diseases* 79, no.4 (April 2024): 990–998.998.

22. A. S. Rivera, K. J. Pak, M. T. Mefford, and R. C. Hechter, "Use of Tenofovir Alafenamide Fumarate for HIV Pre-Exposure Prophylaxis and Incidence of Hypertension and Initiation of Statins," *JAMA Network Open* 6, no. 9 (2023): e2332968.

23. D. Kwarisiima, M. Atukunda, A. Owaraganise, et al., "Hypertension Control in Integrated HIV and Chronic Disease Clinics in Uganda in the SEARCH Study," *BMC Public Health* 19, no. 1 (2019): 511.

24. L. B. Rethy, M. J. Feinstein, C. J. Achenbach, et al., "Antihypertensive Class and Cardiovascular Outcomes in Patients With HIV and Hypertension," *Hypertension* 77, no. 6 (2021): 2023–2033.

25. D. L. Jacobson, A. M. Tang, D. Spiegelman, et al., "Incidence of Metabolic Syndrome in a Cohort of HIV-Infected Adults and Prevalence Relative to the US Population (National Health and Nutrition Examination Survey)," *JAIDS Journal of Acquired Immune Deficiency Syndromes* 43, no. 4 (2006): 458–466.

26. R. Palacios, J. Santos, M. González, J. Ruiz, and M. Márquez, "Incidence and Prevalence of the Metabolic Syndrome in a Cohort of Naive HIV-Infected Patients: Prospective Analysis at 48 Weeks of Highly Active Antiretroviral Therapy," *International Journal of STD & AIDS* 18, no. 3 (2007): 184–187.

27. B. Hansen, J. Petersen, S. Haugaard, et al., "The Prevalence of Metabolic Syndrome in Danish Patients With HIV Infection: The Effect of Antiretroviral Therapy," *HIV Medicine* 10, no. 6 (2009): 378–387.

28. P. Y. Wu, C. C. Hung, W. C. Liu, et al., "Metabolic Syndrome Among HIV-Infected Taiwanese Patients in the Era of Highly Active Antiretroviral Therapy: Prevalence and Associated Factors," *Journal of Antimicrobial Chemotherapy* 67, no. 4 (2012): 1001–1009.

29. S. Sears, J. R. Buendia, S. Odem, et al., "Metabolic Syndrome Among People Living With HIV Receiving Medical Care in Southern United States: Prevalence and Risk Factors," *AIDS and Behavior* 23, no. 11 (2019): 2916–2925.

30. L. W. Ang, O. T. Ng, I. C. Boudville, Y. S. Leo, and C. S. Wong, "An Observational Study of the Prevalence of Metabolic Syndrome in Treatment-Experienced People Living With HIV in Singapore," *PLoS One* 16, no. 6 (2021): e0252320.

31. J. Jumare, P. Dakum, N. Sam-Agudu, et al., "Prevalence and Characteristics of Metabolic Syndrome and Its Components Among Adults Living With and Without HIV in Nigeria: A Single-Center Study," *BMC Endocrine Disorders* 23, no. 1 (2023): 160.

32. O. E. Ayodele, A. O. Akinboro, S. O. Akinyemi, et al., "Prevalence and Clinical Correlates of Metabolic Syndrome in Nigerians Living With Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome," *Metabolic Syndrome and Related Disorders* 10, no. 5 (2012): 373–379.