Higher Income Inequality is Associated with Lower Cumulative Antiretroviral Adherence

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ABSTRACT

Background: Tenofovir diphosphate (TFV-DP) in dried blood spots (DBS) is associated with viral suppression and predicts future viremia. However, its association with social determinants of health (SDoH) in people living with HIV (PLWH) has not been evaluated.

Methods: DBS for TFV-DP were prospectively collected from a clinical cohort of PLWH receiving tenofovir disoproxil fumarate (TDF)-based therapy (up to 3 visits over 48-weeks between 2014 and 2017). Zip code was collected at enrollment and matched with the relevant SDoH data from 2016 obtained from AIDSVu (aidsvu.org). SDoH data included household income, percent living in poverty, education level and income inequality (the latter was quantified using the Gini coefficient, where 0 and 1 represent absolute income equality and inequality, respectively). Log-transformed TFV-DP concentrations were analyzed using a mixed-effects model. Baseline statistics are presented as median (interquartile range). Model results are percent change [95% confidence interval] in TFV-DP for every significant change in the SDoH. All results are reported with no adjustment for multiple comparisons.

Results: A total of 950 person-visits from 430 participants were analyzed, encompassing zip codes within the following Colorado counties: Denver, Arapahoe, Jefferson, Adams and Douglas. Baseline household income, Gini and TFV-DP concentration were $56,227 ($46,500, $70,369), 0.418 (0.391, 0.487) and 1632 (1156, 2323) fmol/punch, respectively. After adjusting for age, sex, race, estimated glomerular filtration rate, body mass index, hematocrit, CD4+ T-cell count, antiretroviral drug class and 3-month self-reported adherence, Gini was inversely associated with TFV-DP in DBS. For every 0.1 increase in Gini, TFV-DP concentration decreased by 9.2% [0.5, 17.1%; P=0.039]. Gini remained significant after adjusting for HIV viral suppression with the same 0.1 increase estimating a decrease of 8.7% [0.3 16.4%; P=0.042] in TFV-DP concentrations. No statistically significant associations were identified between TFV-DP concentration and the other SDoH (Table 2).

Conclusions: Greater income inequality was associated with lower TFV-DP concentrations in PLWH on TDF, suggesting that adherence may be influenced by population level characteristics that exist in the presence of income inequality and impact individual level health outcomes. Future studies on the utility of this adherence biomarker to improve clinical care and adherence in marginalized PLWH are needed.

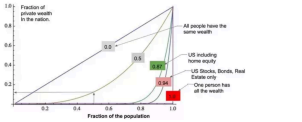
BACKGROUND and OBJECTIVE

- **Studying the social determinants of health (SDoH)+ is a critical component to developing better plans of care and reduction of overall disease burden.**
- **Previous research acknowledges that behavior changes and antiretroviral therapy (ART) alone do not address the social disparities that prevent further reduction of HIV and AIDS.[1]**
- **Therefore, better understanding the association between social determinants and clinically relevant outcomes in HIV therapy will be critical to end the HIV epidemic.**
- **Although previous research has recognized the impact of SDoH on adherence and viral suppression, most studies quantified adherence through self-reporting.[2] In this study, we evaluate the association of SDoH with ART adherence using a novel method to quantify drug adherence and exposure.**

METHODS

- **DBS for TFV-DP were prospectively collected from a clinical cohort of PLWH receiving tenofovir disoproxil fumarate (TDF)-based therapy (up to 3 visits over 48-weeks between 2014 and 2017). TFV-DP was quantified using a validated LC-MS/MS method[3].**
- **Zip code was collected at enrollment and matched with the relevant SDoH data from 2016 obtained from AIDSVu (aidsvu.org).**
- **SDoH data included household income, percent living in poverty, education level and income inequality (the latter was quantified using the Gini coefficient, where 0 represents absolute equality and 1 represents one person having all the wealth).**

Figure 1. U.S. Wealth Inequality Defined by Gini Coefficient.[4]



- **Log-transformed TFV-DP concentrations were analyzed using a mixed-effects model. Baseline statistics are presented as median (IQR).**

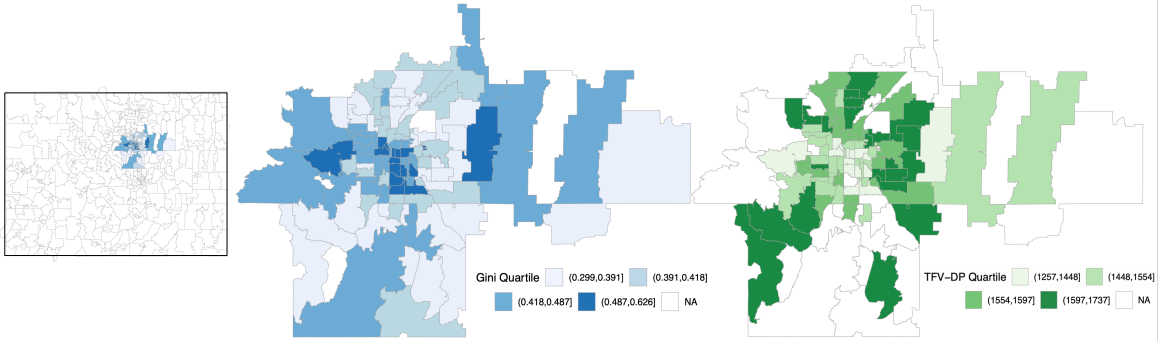
RESULTS

Table 1. Demographics of the study population.

Characteristic	Participants Included in Analysis (n = 430) No. (%) or Median (IQR)
Age	45 (36, 52)
Gender	
Female	66 (15%)
Male	364 (85%)
Race/ethnicity	
Black	96 (22%)
White	233 (54%)
Hispanic	83 (19%)
Other	18 (4%)
Body Mass Index (Kg/m^2)	
<18.5	18 (4%)
18.5-25	179 (42%)
25-30	143 (33%)
>30	90 (21%)
eGFR (mL/min)	88 (74, 104)
Hematocrit	45 (42, 47)
CD4$^+$ T-cell count (cells/mm^3)	
<200	48 (11%)
200-350	59 (14%)
350-500	67 (16%)
>500	256 (60%)
ART Drug Class	
NNRTI-based	112 (26%)
INSTI-based	158 (37%)
b/PI-based	109 (25%)
Multiclass	51 (12%)
HIV Viral Load	
Viremic: VL>=200	130 (30%)
Suppressed: VL [20,200)	5 (1%)
Suppressed: VL<20	295 (69%)
3-month self-reported adherence (%)	98% (90%, 100%)

RESULTS (cont'd)

Figure 2. Gini Coefficient (blue) and Estimated** TFV-DP Concentration (green) According to Zip Code of Study Population in the State of Colorado.

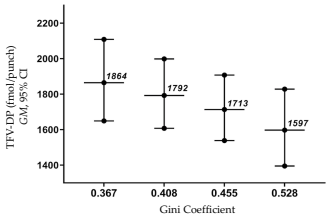


**Population fitted values from unadjusted mixed-effects model.

Table 2. Percent Change in TFV-DP Concentration in DBS (fmol/punch) for Change in Analyzed in Each Social Determinant of Health.

Social Determinant Of Health Indicator	Adjusted* Percent change in TFV-DP concentration in DBS (fmol/punch)	95% CI	p-value
0.1 increase in income inequality (Gini coefficient)	-9.2%	(-17.1, -0.5%)	0.039
10% increase in population living in poverty	1.9%	(-6.0, 10.5%)	0.65
10% increase in persons with high school diploma or equivalent	-3.5%	(-8.8, 2.1%)	0.22
$10,000 increase in median household income	-0.2%	(-3.3, 3.0%)	0.90

Figure 3. Adjusted* TFV-DP Concentrations by Gini Coefficient.



Covariates set to:
1. Age: 45 years
2. Gender: male
3. Race: white
4. BMI: 25 Kg/m^2
5. HCT: 45%
6. eGFR: 88 mL/min/1.73m^2
7. CD4$^+$ T-cells: 575 cells/mm3
8. ART anchor drug class: INSTI
9. Three-month self-reported adherence: 98%

*Adjusted for age, sex, race, estimated glomerular filtration rate, body mass index, hematocrit, CD4+ T cell count, antiretroviral drug class, and 3-month self-reported adherence. All results are reported with no adjustment for multiple comparisons.

CONCLUSIONS

- **Greater income inequality was associated with lower TFV-DP concentrations in PLWH on TDF, suggesting that adherence may be influenced by population level characteristics that exist in the presence of income inequality and impact individual level health outcomes.**
- **Understanding non-biological, social factors that impact ART adherence could play a critical role in the development of more individualized strategies to improve clinical care in HIV.**
- **Extending individual-level clinical and objective measures of adherence to include population-level measures will be indispensable to understand the impact of community-wide SDoH on ART adherence. Future research to understand how to best implement these findings into clinical practice and reduce the burden of HIV disease in the community is needed.**

REFERENCES

1. *De Jesus, M. and D.R. Williams, The Care and Prevention in the United States Demonstration Project: A Call for More Focus on the Social Determinants of HIV/AIDS. Public Health Reports, 2018. 133(2_suppl): p. 28S-33S.*
2. *Bradley, E.L.P., et al., Psychological and social determinants of health, antiretroviral therapy (ART) adherence, and viral suppression among HIV-positive black women in care. AIDS Care, 2019. 31(8): p. 932-941.*
3. *Castillo-Mancilla JR, Zheng JH, Rower JE, et al. Tenofovir, emtricitabine, and tenofovir diphosphate in dried blood spots for determining recent and cumulative drug exposure. AIDS Res Hum Retroviruses 2013;29:384-390.*
4. *https://www.quora.com/How-accurate-and-representative-is-the-Gini-coefficient*

+SDoH are defined as "the conditions in which people are born, grow, live, work and age, as well as the complex, interrelated social structures and economic systems that shape these conditions. SDoH include aspects of the social environment (e.g., discrimination, income, education level, marital status), the physical environment (e.g., place of residence, crowding conditions, built environment [i.e., buildings, spaces, transportation systems, and products that are created or modified by people]), and health services (e.g., access to and quality of care, insurance status). (CDC)