Low-Density Lipoprotein Changes in People with HIV Initiating Statins for Primary Prevention

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Background

CVD Risk in PWH	↑ Cholesterol in PWH	Statins in PWH	Lipids Control in PWH
Up to 2x as high as general population[1]	>30% prevalence[2] Accounts for 44% of MIs[3]	Recommended for all PWH aged 40–75 with 10-year CVD risk ≥5%[4,5]	Suboptimal cholesterol reductions after statin initiation[6–9]

- Statin use will likely increase in PWH at low-to-moderate CVD risk given the findings of the REPRIEVE trial and new statin therapy guidelines for PWH.[4,5]
- Clinical benefit of statins may be lower than expected with insufficient LDL reductions.
- Older studies reported smaller LDL reductions for PWH vs. without HIV, with less than half of PWH having 1-year LDL reductions ≥30%, and only 50–70% meeting cholesterol targets.[6–9]

Objective

- Examine LDL changes in PWH initiating statins for primary prevention in a US clinical cohort

Abbreviations: CVD, cardiovascular disease; LDL, low-density lipoprotein; MI, myocardial infarction; PWH, persons with HIV.

Methods

Study Population

- **CNICS**: clinical cohort of PWH at 8 academic centers in the US
  - PWH initiating statin therapy in 2014–2022 (first prescription in the EHR)
  - No CVD history (excluded PWH with prior MI, stroke, PCI, or CABG)

Analytic Approach

Outcome Definition	Measure	Statistical Method
Absolute and relative LDL change from baseline	1-year change estimated from model	Linear regression with GEE and time on statins as a linear predictor
First LDL showing ≥30% reduction from baseline	1-year cumulative incidence (CI)	Kaplan-Meier curves

- **Multiple imputation** for PWH missing baseline LDL (17%)
  - Imputed 50 data sets with MCMC based on baseline demographic and clinical characteristics
- **Censored** at death, 12 months with no HIV visit or lab, or site-specific data end date (2023–2024), whichever occurred first
- **Intention-to-treat** (ignored statin therapy changes and discontinuations)

Abbreviations: CABG, coronary artery bypass graft; GEE, generalized estimating equations; MCMC, Markov Chain Monte Carlo; PCI, percutaneous coronary intervention.

Results

- We included 4,334 PWH who were 80% cis men and 46% Black, 41% White , and 9% Hispanic PWH (**Table 1**).
- CVD risk factors included hypertension (59%), obesity (39%), diabetes (25%), and LDL >190 mg/dL (6%).

Table 1. Characteristics of 4,334 PWH initiating a statin, CNICS, 2014–2022.

Characteristic at Statin Initiation	N (%) or median (IQR)
Gender	
Cisgender men	3,470 (80%)
Cisgender women	828 (19%)
Transgender	36 (1%)
Race/ethnicity	
Black, not Hispanic	1,992 (46%)
Hispanic, any race	400 (9%)
White, not Hispanic	1,779 (41%)
Other groups	163 (4%)
Age, years	54 (47, 59)
Calendar Year	2018 (2016, 2020)
HIV RNA <200 copies/mL	3,987 (92%)
CD4 count, cells/μL	638 (417, 905)
LDL cholesterol, mg/dL	125 (97, 153)
Total cholesterol, mg/dL	208 (175, 240)
Triglycerides, mg/dL	164 (111, 250)
Body mass index ≥30 kg/m^2	1,702 (39%)
Diabetes mellitus	1,082 (25%)
Hypertension	2,537 (59%)

Diabetes was defined as either 1) A1c ≥6.5%, 2) diabetes-specific medication prescription, or 3) diabetes-related medication prescription with a diagnosis. Hypertension was defined as an antihypertensive prescription with a diagnosis.

- The most commonly prescribed initial statins were atorvastatin (64%), pravastatin (16%), and rosuvastatin (16%).
- At 6 sites with dosage data (N=2979), 8%, 72%, and 21% initiated low-, medium-, and high-intensity statin therapy, respectively.
- PWH contributed 15,874 person-years of follow-up before meeting censoring criteria, with a median of 3.2 person-years (IQR 1.6, 5.3) per patient.
- 3,836 (89%) of PWH had ≥1 repeat LDL test before censoring, and these PWH had a median of 4 LDL tests (IQR 2, 7) that were a median of 7 months (IQR 4, 12) apart.
- After 1 year, among all PWH, the mean absolute change in LDL was -33.5 mg/dL (95% CI -35.2, -31.9), or a relative change of -21.8% (95% CI -23.0%, -20.6%), and 35.5% (95% CI 34.0%, 37.0%) of PWH had an LDL reduction ≥30% (**Table 2**).
- PWH with higher baseline LDL and those initiating higher-intensity statin therapy had greater LDL reductions and cumulative incidence of LDL reduction ≥30% at 1 year (**Table 2**).

Table 2. Unadjusted 1-year LDL changes in persons with HIV initiating statins, 2014–2022

Patient Group	N	1-Year Absolute LDL Change (mg/dL)	1-Year Relative LDL Change (%)	1-Year Cumulative Incidence of LDL Reduction ≥30%
All PWH	4334	-33.5 (-35.2, -31.9)	-21.8% (-23.0%, -20.6%)	35.5% (34.0%, 37.0%)
By baseline LDL (mg/dL)				
<100	1189	-3.7 (-5.9, -1.6)	-2.5% (-5.7%, +0.6%)	19.6% (17.2%, 22.0%)
100–190	2869	-38.6 (-40.2, -36.9)	-26.8% (-28.0%, -25.7%)	39.8% (37.9%, 41.7%)
>190	276	-89.6 (-99.1, -80.0)	-39.5% (-42.8%, -36.3%)	59.5% (52.9%, 66.0%)
By statin intensity [a]				
Low	230	-19.1 (-24.2, -13.9)	-11.9% (-16.1%, -7.8%)	21.8% (16.2%, 27.4%)
Moderate	2134	-33.3 (-35.5, -31.2)	-22.1% (-23.7%, -20.6%)	37.2% (35.0%, 39.3%)
High	615	-39.7 (-44.7, -34.6)	-26.8% (-30.8%, -22.8%)	41.6% (37.5%, 45.8%)

[a] Restricted to 2979 patients at 6 sites with statin dosage data.

Conclusions

- At 1 year after statin initiation, PWH at 8 clinical sites had a mean LDL reduction of 22%, with about ⅓ having a reduction ≥30%.
- Even among PWH on high-intensity statins, less than half had an LDL reduction ≥30% at 1 year.
- Patient non-adherence, lack of statin dose up-titration, and true statin non-response despite adherence may have played a role.
- Efforts are needed to elucidate and address drivers of inadequate LDL reductions in PWH.

Considerations

- LDL was measured inconsistently during follow-up; PWH with no repeat LDL were censored.
- Our analyses did not account for statin therapy interruptions or adherence.

Next steps

- Examine % of PWH meeting LDL targets
- Analyses stratified by CVD risk, statin indication
- Identify predictors of smaller LDL reductions
- Analyses accounting for lack of repeat LDL labs

Acknowledgements

References: **1.** Shah et al. Circulation. 2018;138(11):1100–1112. **2.** Collins et al. JAMA Netw Open. 2023;6(8):e2327584. **3.** Althoff et al. Lancet HIV. 2019;6(2):e93–e104. **4.** Grinspoon et al. N Engl J Med. 2023;389(8):687–699. **5.** US DHHS. **6.** Silverberg et al. Ann Intern Med. 2009;150(5):301–13. **7.** Singh et al. Clin Infect Dis. 2011;52(3):387–95. **8.** Levy et al. AIDS Patient Care STDS. 2018; 32(2):58–69. **9.** Burkholder et al. J Clin Lipidol. 2018;12(4):988–998.

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