HHS Public Access

Author manuscript

AIDS. Author manuscript; available in PMC 2021 September 09.

Published in final edited form as:

AIDS. 2019 October 01; 33(12): 1935–1942. doi:10.1097/QAD.0000000000002304.

Excess heart age in adult outpatients in routine HIV care

Angela M. Thompson-Paul[a], **Frank J. Palella Jr**[b], **Nabil Rayeed**[c], **Matthew D. Ritchey**[a], **Kenneth A. Lichtenstein**[d], **Deesha Patel**[e], **Quanhe Yang**[a], **Cathleen Gillespie**[a], **Fleetwood Loustalot**[a], **Pragna Patel**[f], **Kate Buchacz**[e], **HIV Outpatient Study Investigators**[*]

[a]Division for Heart Disease and Stroke Prevention, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia

[b]Feinberg School of Medicine, Northwestern University, Chicago, Illinois

[c]Cerner Corporation, Kansas City, Missouri

[d]Eisenhower Medical Center, Palm Springs, California

[e]Division of HIV/AIDS Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, & TB Prevention, Centers for Disease Control and Prevention, Atlanta

[f]Division of Global Health Protection, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

Abstract

Objective: Cardiovascular disease (CVD) is a common cause of morbidity and mortality among persons living with HIV (PLWH). We used individual cardiovascular risk factor profiles to estimate heart age for PLWH in medical care in the United States.

Design: Cross-sectional analyses of HIV Outpatient Study (HOPS) data

Methods: Included in this analysis were participants aged 30–74 years, without prior CVD, with at least two HOPS clinic visits during 2010–2017, at least 1-year of follow-up, and available covariate data. We calculated age and race/ethnicity-adjusted heart age and excess heart age (chronological age – heart age), using a Framingham risk score-based model.

Results: We analyzed data from 2467 men and 619 women (mean chronologic age 49.3 and 49.1 years, and 23.6% and 54.6% Non-Hispanic/Latino black, respectively). Adjusted excess heart age was 11.5 years (95% confidence interval, 11.1–12.0) among men and 13.1 years (12.0–14.1)

Correspondence to Angela M. Thompson-Paul, PhD, MSPH, LCDR, U.S. Public Health Service, Epidemiologist, Division for Heart Disease and Stroke Prevention, Centers for Disease Control and Prevention, 4700 Buford Hwy NE, MS F-73, Atlanta, GA 30341, USA. Tel: +1 770 488 8536; eup4@cdc.gov.

[*]Investigators listed in the Appendix.

Authors' contributions: All authors contributed to the writing of this article. A.M.T., M.D.R., F.L., and K.B. conceived the idea. F.J.P. and K.L. contributed to the study design and collection of data. N.R. and A.M.T. were responsible for analysis and interpretation of the data under the guidance of C.G., Q.Y., M.D.R., and K.B. A.M.T. wrote all major drafts of the article with critical input from F.J.P., M.D.R., K.L., D.P., Q.Y., F.L., P.P., and K.B. All authors have reviewed and approved the article.

Conflicts of interest

F.P. has served on the Advisory Board for Gilead Sciences and Janssen Pharmaceuticals; speakers bureau for Gilead Sciences, Janssen Pharmaceuticals, Merck, and ViiV. K.L. has served on the Advisory Board for Gilead Sciences, received research support from AbbVie and Gilead Sciences, and has given CME Lectures for Simply Speaking and Integrity. All other authors declare that no competing interests exist.

among women. Excess heart age was seen among all age groups beginning with persons aged 30–39 years [men, 7.8 (6.9–8.8); women, 7.7 (4.9–10.4)], with the highest excess heart age among participants aged 50–59 years [men, 13.7 years (13.0–14.4); women, 16.4 years (14.8–18.0)]. More than 50% of participants had an excess heart age of at least 10 years.

Conclusions: Excess heart age is common among PLWH, begins in early adulthood, and impacts both women and men. Among PLWH, CVD risk factors should be addressed early and proactively. Routine use of the heart age calculator may help optimize CVD risk stratification and facilitate interventions for aging PLWH.

Keywords

cardiovascular disease; cardiovascular risk score; heart age; HIV

Introduction

Persons living with HIV (PLWH) have a higher risk of cardiovascular disease (CVD) events [1-6] and an increased prevalence of certain risk factors [1,7-9] and comorbid conditions [10,11] than persons without HIV. Healthcare providers now must routinely consider these factors in the long-term care of PLWH [12,13]. CVD risk prediction tools are clinically useful and have long been used to guide recommendations for medication therapy or other preventive interventions [14-18]; however, they underestimate risk in PLWH [19-21]. ‘Heart age’ is an alternative and potentially easier concept to understand and interpret [22,23], using a patient’s cardiovascular risk factor profile to estimate their vascular system’s age [14,24].

This analysis provides the first estimates of heart age in a large, diverse cohort of PLWH in the United States (US). Our objectives were to calculate heart age for PLWH by select sociodemographic and clinical characteristics and to examine correlations between two different heart age model estimates.

Methods

Study population

We analyzed data from the HIV Outpatient Study (HOPS), an ongoing, prospective cohort study of PLWH aged at least 18 years receiving care at public and private HIV clinics in the United States, described in detail elsewhere [1,25]. Ethical review board at the Centers for Disease Control and Prevention approved the protocol and all study participants provided written informed consent.

From among 4358 HOPS participants seen during 1 January 2010 to 31 December 2017, we analyzed data for 3086 participants. We serially excluded 1272 (29.2%) for the following reasons: had fewer than two HOPS encounters ($n = 13$), lacked at least 1 data element required for calculation of heart age ($n = 404$), were pregnant ($n = 3$), not aged 30–74 years (heart age equations are validated only for persons in this age range, $n = 540$), or had prior stroke, myocardial infarction, or coronary heart disease ($n = 312$).

Outcome and predictor variables

Heart age was calculated as the 'age of a person with the same predicted risk but with all other risk factors in the normal range' [14]. Excess heart age was calculated as the difference between an individual's heart and chronologic ages and represents the excess risk for CVD events [24]. We used two models to calculate heart age. The cholesterol-based ('laboratory-based') model [14] included the following covariates: SBP, antihypertensive medication use, diabetes mellitus status, smoking status, age, sex, total blood cholesterol, and high-density lipoprotein (HDL) cholesterol. The BMI-based model ('nonlaboratory' or 'office-based model') included the same covariates except used BMI in place of total and HDL cholesterol [14,24].

We performed cross-sectional data analyses, defining the index visit for each patient as the most recent visit between 1 January 2010 and 31 December 2017 at which at least one total cholesterol value and at least 365 days of follow-up after the index visit were available. Sociodemographic characteristics, CVD risk factors, and HIV-related factors were collected from the index visit, or from medical encounter(s) that were within the window of observation (i.e. 1 year before through 1 year after the index visit).

Statistical analyses

Due to sociodemographic differences in men and women with HIV and sex-specific differences in CVD risk factors, all analyses were conducted separately for men and women [1,6,9,26]. We calculated age-adjusted and race/ethnicity-adjusted mean chronological age, heart age, excess heart age and the prevalence of excess heart age at least 10 years. Using the Pearson correlation coefficient (ρ), we examined linear correlations between estimates derived using the cholesterol- and BMI-based models. Repeating these analyses, we age-standardized the results to the US 2010 Census population to examine heart age among HOPS participants as though they had an age distribution similar to the U.S. population. Statistical analyses were performed using SAS 9.3 (SAS Institute, Cary, North Carolina, USA), and P values less than 0.05 were considered statistically significant.

Results

Population characteristics

Among 2467 men and 619 women included in our analytic sample, the majority of men were non-Hispanic/Latino white (52.7%) and had more than a high school education (54.4%). The majority of women were non-Hispanic/Latino black (54.6%) and had a high school education or less (55.7%) (Table 1).

Heart age and excess heart age results

The mean chronological age in the cohort was 49.3 years in men (heart age: 60.8 years; excess heart age: 11.5 years; Table 2) and 49.1 years in women (heart age: 62.2 years; excess heart age: 13.1 years). Mean excess heart age was the lowest among the youngest age group (30–39 years), although it still exceeded chronological age by 7.8 years [95% confidence interval (CI: 6.9–8.8)] for men and 7.7 years (4.9–10.4) for women. Excess heart age was greatest among PLWH aged 50–59 years [men: 13.7 (13.0–14.4); women:

16.4 (14.8–18.0)], and those who reported cholesterol-lowering medication (i.e. statin) use [men: 15.1 (14.0–16.1); women: 18.6 (16.6–20.6)] or aspirin use [men: 16.1 (14.7–17.6); women: 19.4 (16.7–22.1)]; and men with hepitatis-C virus (HCV) co-infection [13.3 years (12.3–14.3)] or less than a high school education [13.9 (12.5–15.3)]. Heart age exceeded chronological age by at least 10 years among 53.1% of men and 59.3% of women studied.

Comparative results using two methods for heart age estimation

There was a strong linear correlation between excess heart age estimates using the cholesterol-based and BMI-based models (men, $\rho = 0.87$; women, $\rho = 0.84$), with similar estimates of mean excess heart age (men: 11.5 and 11.6 years; women: 13.1 and 13.8 years; cholesterol-based and BMI-based models, respectively). Results were modestly attenuated when age-standardized to the 2010 US Census population (men, 11.3 and 11.5 years; women, 12.6 and 13.2 years; cholesterol-based and BMI-based models, respectively), but heart age still exceeded chronological age in all categories for men and women (results not shown).

Discussion

Among PLWH, heart age exceeded chronological age by a mean of 11.5 years for men and 13.1 years for women and was at least 10 years among more than half of all participants. We identified a high correlation of excess heart age estimates between the cholesterol-based and BMI-based models, which may represent the first study to do so.

Our excess heart age estimates exceeded those of the general US population [men: 7.8 years; women: 5.4 years using 2011–2013 Behavioral Risk Factor Surveillance Survey (BRFSS) data], and those reported from a small sample of New York PLWH (7.2 years) with clinical visits between 2004 and 2009 [10]. Our findings were consistent with estimates of excess heart age in some subpopulations, for example, non-Hispanic black men (11.0 years) and women (11.1 years) [24], men and women with diabetes [24], and populations with chronic HCV, or HIV/HCV co-infection (12.5 and 9.6 years, respectively) [10], all calculated using the BMI-based model. Excess heart age emerged at younger ages among PLWH compared with the general US population (e.g. among 30–39 year olds: 7.8 and 7.7 years for men and women in the HOPS compared with 3.8 and −0.3 years for men and women in the general US population) but was consistent with increased estimates of excess heart age among similarly aged adults with diabetes (men: 4 years; women: 8 years) [24]. Excess heart age was particularly high among women with HIV where it consistently exceeded that of men with HIV across key sociodemographic and clinical characteristics. Compared with men, women in the HOPS had higher prevalence of certain CVD risk factors, more advanced HIV disease stage, and lower prevalence of HIV viral suppression. Factors, such as early menopause, increased inflammation and immune activation, and differing plaque morphology [26-29] may have contributed to the higher excess heart age among women in our study; however, the etiological basis for increased CVD risk in women living with HIV is unclear.

Despite having greater heart age than the general population, PLWH may have been less likely than patients without HIV to be prescribed medication for CVD risk factor

management [30]. Guidelines for CVD risk factor management are well established for the general population [31], but there is evolving guidance around recommended medication therapy for chronic disease management among PLWH, which recommends blood pressure and lipid management, whenever clinically feasible [32,33]. These recommendations were based on previously published national guidelines and are not specific for the PLWH population [31,34,35]. Updated national guidelines for cholesterol management acknowledged HIV as an atherosclerotic CVD 'risk enhancer' for the first time in 2018 [36]. Vascular aging may occur earlier among PLWH [37], atherosclerotic plaque morphology may differ [38,39], and sex-specific risk may present differently compared with the general population; therefore, differences in recommendations, such as lower age thresholds for statin therapy initiation may be needed.

Statin use appears to reduce mortality among PLWH [40,41], but a dearth of clinical trial data related to the safety and efficacy of statins in this population has left clinicians without clear guidance on the type and dose of statin to prescribe [42]. Two ongoing multicenter studies, the Elite Controller and ART-Treated HIV+ Statin Versus ASA Treatment Intervention Study (https://clinicaltrials.gov/ct2/show/NCT02081638) and the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) [43], may inform CVD prevention in PLWH. Future guidelines will need to consider available evidence as well as national guidelines for hypertension, high blood cholesterol, and lifestyle management to reduce CVD risk, and their implications for HIV-treatment algorithms [35]. Furthermore, they could emphasize use of team-based models of care, previously shown to be effective for the support of blood pressure control and for integrated HIV care [44,45].

Important among our findings was the high correlation in excess heart age estimates between the two models used, suggesting that either the cholesterol-based or BMI-based method could be used to estimate heart age in PLWH. This finding may be especially important for resource-constrained medical settings where BMI may be easier to routinely measure than blood cholesterol levels. One study reported high correlation in results from Framingham equations using BMI or blood cholesterol to estimate cardiovascular risk in PLWH from Cote d'Ivoire [46].

Despite giving unique insight to CVD risk among PLWH, our analysis is subject to several limitations. HOPS participants included in this analysis were older, had more advanced HIV, and more chronic comorbidities than excluded participants (data not shown). We excluded 24.8% of participants with prior CVD from this analysis, compared with 7.6% of participants excluded in a similar study in the general US population [24] underscoring the greater risk for developing CVD among PLWH. On the basis of on established CVD risk functions [14,47], which were not validated for use in PLWH, heart age calculations may underestimate CVD risk in this population [19-21,48]. Despite limitations and in the absence of tools validated for use in PLWH, the heart age calculator may give healthcare providers an easy-to-understand and readily available tool (https://www.cdc.gov/vitalsigns/cardiovasculardisease/heartage.html) with which to discuss heart health with PLWH.

Conclusions

The burden of excess heart age is common among PLWH, begins in early adulthood, and impacts both men and women. High correlation of results between the cholesterol-based and BMI-based heart age estimation models suggests that either method could be used for care management of PLWH. Among PLWH, CVD risk factors should be addressed early and proactively. Routine use of the heart age calculator may help optimize CVD risk stratification and facilitate interventions for aging PLWH.

Acknowledgements

Funding:

This work was supported by the Centers for Disease Control and Prevention (contract nos. 200-2001-00133, 200-2006-18797 and 200-2011-41872).

Disclaimer:

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Appendix

The HIV Outpatient Study (HOPS) Investigators currently include the following persons and sites:

Kate Buchacz, Marcus D. Durham, Jun Li, Division of HIV/AIDS Prevention, National Center for HIV, Viral Hepatitis, STD, and TB Prevention (NCHHSTP), Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, USA; Cheryl Akridge, Stacey Purinton, Nabil Rayeed, Selom Agbobil-Nuwoaty, Kalliope Chagaris, Kimberly Carlson, Carl Armon, Linda Battalora, Jonathan Mahnken Cerner Corporation, Kansas City, Missouri, USA; Frank J. Palella, Saira Jahangir, Conor Daniel Flaherty, Patricia Bustamante, Feinberg School of Medicine, Northwestern University, Chicago, Illinois, USA; John Hammer, Kenneth S. Greenberg, Barbara Widick, Rosa Franklin, Rocky Mountain Cares, Denver, CO; Douglas J. Ward, Troy Thomas, Cheryl Stewart, Dupont Circle Physicians Group, Washington, DC, USA; Jack Fuhrer, Linda Ording-Bauer, Rita Kelly, Jane Esteves, State University of New York (SUNY), Stony Brook, New York, USA; Ellen M. Tedaldi, Ramona A. Christian, Faye Ruley, Dania Beadle, Princess Davenport, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania, USA; Richard M. Novak, Andrea Wendrow, Stockton Mayer. University of Illinois at Chicago, Chicago, Illinois, USA; Mia Scott, Billie Thomas, Loraine Van Slyke APEX Family Medicine, Denver, Colorado, USA; Cynthia Mayer, Terry Beitler, Karen Maroney, Denise Franklin, SJH Comprehensive Research Institute, Tampa, Florida, USA.

References

1. Buchacz K, Baker RK, Palella FJ Jr, Shaw L, Patel P, Lichtenstein KA, et al., HIV Outpatient Study Investigators. Disparities in prevalence of key chronic diseases by gender and race/ethnicity among antiretroviral-treated HIV-infected adults in the US. Antivir Ther2013; 18:65–75. [PubMed: 23111762]

2. Drozd DR, Kitahata MM, Althoff KN, Zhang J, Gange SJ, Napravnik S, et al.Increased risk of myocardial infarction in HIV-infected individuals in North America compared with the general population. J Acquir Immune Defic Syndr2017; 75:568–576. [PubMed: 28520615]

3. Freiberg MS, Chang CC, Kuller LH, Skanderson M, Lowy E, Kraemer KL, et al.HIV infection and the risk of acute myocardial infarction. JAMA Intern Med2013; 173:614–622. [PubMed: 23459863]

4. Paisible AL, Chang CC, So-Armah KA, Butt AA, Leaf DA, Budoff M, et al.HIV infection, cardiovascular disease risk factor profile, and risk for acute myocardial infarction. J Acquir Immune Defic Syndr2015; 68:209–216. [PubMed: 25588033]

5. Womack JA, Chang CC, So-Armah KA, Alcorn C, Baker JV, Brown ST, et al.HIV infection and cardiovascular disease in women. J Am Heart Assoc2014; 3:e001035. [PubMed: 25324353]

6. Triant VA. Cardiovascular disease and HIV infection. Curr HIV/AIDS Rep2013; 10:199–206. [PubMed: 23793823]

7. Mdodo R, Frazier EL, Dube SR, Mattson CL, Sutton MY, Brooks JT, Skarbinski J. Cigarette smoking prevalence among adults with HIV compared with the general adult population in the United States. Ann Intern Med2015; 162:335–344. [PubMed: 25732274]

8. Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. J Clin Endocrinol Metab2007; 92:2506–2512. [PubMed: 17456578]

9. Thompson-Paul AM, Wei SC, Mattson CL, Robertson M, Hernandez-Romieu AC, Bell TK, et al.Obesity among HIV-infected adults receiving medical care in the United States: data from the cross-sectional Medical Monitoring Project and National Health and Nutrition Examination Survey. Medicine (Baltimore)2015; 94:e1081. [PubMed: 26166086]

10. Kakinami L, Block RC, Adams MJ, Cohn SE, Maliakkal B, Fisher SG. Risk of cardiovascular disease in HIV, hepatitis C, or HIV/hepatitis C patients compared to the general population. Int J Clin Pract2013; 67:6–13. [PubMed: 23241046]

11. Wong C, Gange SJ, Moore RD, Justice AC, Buchacz K, Abraham AG, et al., North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD). Multimorbidity among persons living with HIV in the U.S. Clin Infect Dis2017; 66:1230–1238.

12. Lundgren JD, Battegay M, Behrens G, De Wit S, Guaraldi G, Katlama C, et al., EACS Executive Committee. European AIDS Clinical Society (EACS) guidelines on the prevention and management of metabolic diseases in HIV. HIV Med2008; 9:72–81. [PubMed: 18257770]

13. Dubé MP, Stein JH, Aberg JA, Fichtenbaum CJ, Gerber JG, Tashima KT, et al.Guidelines for the evaluation and management of dyslipidemia in Human Immunodeficiency Virus (HIV)-Infected adults receiving antiretroviral therapy: recommendations of the HIV Medicine Association of the Infectious Disease Society of America and the Adult AIDS Clinical Trials Group. Clin Infect Dis2003; 37:613–627. [PubMed: 12942391]

14. D'Agostino RB Sr, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, Kannel WB. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation2008; 117:743–753. [PubMed: 18212285]

15. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report. Circulation2002; 106:3143. [PubMed: 12485966]

16. Conroy RM, Pyörälä K, Fitzgerald AP, Sans S, Menotti A, De Backer G, et al., SCORE project group. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. Eur Heart J2003; 24:987–1003. [PubMed: 12788299]

17. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, Sr D'Agostino RB, Gibbons R, et al., American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA Guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation2013; 129 (25 Suppl 2):S49–S73. [PubMed: 24222018]

18. Friis-Moller N, Thiebaut R, Reiss P, Weber R, Monforte AD, De Wit S, et al., DAD study group. Predicting the risk of cardiovascular disease in HIV-infected patients: the data collection on adverse effects of anti-HIV drugs study. European journal of cardiovascular prevention and rehabilitation: official journal of the European Society of Cardiology, Working Groups on

Epidemiology & Prevention and Cardiac Rehabilitation and Exercise Physiology2010; 17:491–501.

19. Thompson-Paul AM, Lichtenstein KA, Armon C, Palella FJ Jr, Skarbinski J, Chmiel JS, et al.Cardiovascular disease risk prediction in the HIV Outpatient Study. Clin Infect Dis2016; 63:1508–1516. [PubMed: 27613562]
20. Triant VA, Perez J, Regan S, Massaro JM, Meigs JB, Grinspoon SK, Sr D'Agostino RB. Cardiovascular risk prediction functions underestimate risk in HIV infection. Circulation2018; 137:2203–2214. [PubMed: 29444987]
21. Feinstein MJ, Nance RM, Drozd DR, Ning H, Delaney JA, Heckbert SR, et al.Assessing and refining myocardial infarction risk estimation among patients with human immunodeficiency virus: a study by the centers for AIDS Research Network of Integrated Clinical Systems. JAMA Cardiol2017; 2:155–162. [PubMed: 28002550]
22. Soureti A, Hurling R, Murray P, van Mechelen W, Cobain M. Evaluation of a cardiovascular disease risk assessment tool for the promotion of healthier lifestyles. Eur J Cardiovasc Prev Rehabil2010; 17:519–523. [PubMed: 20195154]
23. Lopez-Gonzalez AA, Aguilo A, Frontera M, Bennasar-Veny M, Campos I, Vicente-Herrero T, et al.Effectiveness of the Heart Age tool for improving modifiable cardiovascular risk factors in a Southern European population: a randomized trial. Eur J Prev Cardiol2015; 22:389–396. [PubMed: 24491403]
24. Yang Q, Zhong Y, Ritchey M, Cobain M, Gillespie C, Merritt R, et al.Vital Signs: Predicted heart age and racial disparities in heart age among U.S. adults at the state level. MMWR Morb Mortal Wkly Rep2015; 64:950–958. [PubMed: 26335037]
25. Lichtenstein KA, Armon C, Buchacz K, Chmiel JS, Buckner K, Tedaldi EM, et al., HIV Outpatient Study (HOPS) Investigators. Low CD4+ T cell count is a risk factor for cardiovascular disease events in the HIV outpatient study. Clin Infect Dis2010; 51:435–447. [PubMed: 20597691]
26. Foldyna B, Fourman LT, Lu MT, Mueller ME, Szilveszter B, Neilan TG, et al.Sex Differences in subclinical coronary atherosclerotic plaque among individuals with HIV on antiretroviral therapy. J Acquir Immune Defic Syndr 19992018; 78:421–428.
27. Meier A, Chang JJ, Chan ES, Pollard RB, Sidhu HK, Kulkarni S, et al.Sex differences in the Toll-like receptor-mediated response of plasmacytoid dendritic cells to HIV-1. Nature medicine2009; 15:955–959.
28. Fitch KV, Srinivasa S, Abbara S, Burdo TH, Williams KC, Eneh P, et al.Noncalcified coronary atherosclerotic plaque and immune activation in HIV-infected women. J Infect Dis2013; 208:1737–1746. [PubMed: 24041790]
29. Looby SE, Fitch KV, Srinivasa S, Lo J, Rafferty D, Martin A, et al.Reduced ovarian reserve relates to monocyte activation and subclinical coronary atherosclerotic plaque in women with HIV. AIDS2016; 30:383–393. [PubMed: 26696388]
30. Ladapo JA, Richards AK, DeWitt CM, Harawa NT, Shoptaw S, Cunningham WE, et al.Disparities in the quality of cardiovascular care between HIV-infected versus HIV-uninfected adults in the United States: a cross-sectional study. J Am Heart Assoc2017; 6:pii: e007107. [PubMed: 29138182]
31. Stone NJ, Robinson JG, Lichtenstein AH, Bairey Merz CN, Blum CB, Eckel RH, et al., American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol2014; 63 (25 Pt B):2889–2934. [PubMed: 24239923]
32. Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horberg MA, et al., Infectious Diseases Society of America. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis2014; 58:1–10. [PubMed: 24343580]
33. Lucas GM, Ross MJ, Stock PG, Shlipak MG, Wyatt CM, Gupta SK, et al., HIV Medicine Association of the Infectious Diseases Society of America. Clinical practice guideline for the management of chronic kidney disease in patients infected with HIV: 2014 update by the HIV

Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis2014; 59:e96–e138. [PubMed: 25234519]

34. National High Blood Pressure Education Program. The Seventh Report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2004.
35. Eckel RH, Jakicic JM, Ard JD, de Jesus JM, Houston Miller N, Hubbard VS, et al., American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol2014; 63 (25 Pt B):2960–2984. [PubMed: 24239922]
36. Grundy SM, Stone NJ, Bailey AL, Beam C, Birtcher KK, Blumenthal RS, et al.2018AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol2018; 73:3168–3209. [PubMed: 30423391]
37. Cohen J, Torres C. HIV-associated cellular senescence: a contributor to accelerated aging. Ageing Res Rev2017; 36:117–124. [PubMed: 28017881]
38. Zanni MV, Abbara S, Lo J, Wai B, Hark D, Marmarelis E, et al.Increased coronary atherosclerotic plaque vulnerability by coronary computed tomography angiography in HIV-infected men. AIDS2013; 27:1263–1272. [PubMed: 23324657]
39. Zanni MV, Fitch KV, Feldpausch M, Han A, Lee H, Lu MT, et al.2013 American College of Cardiology/American Heart Association and 2004 Adult Treatment Panel III cholesterol guidelines applied to HIV-infected patients with/without subclinical high-risk coronary plaque. AIDS2014; 28:2061–2070. [PubMed: 25265074]
40. Uthman OA, Nduka C, Watson SI, Mills EJ, Kengne AP, Jaffar SS, et al.Statin use and all-cause mortality in people living with HIV: a systematic review and meta-analysis. BMC Infect Dis2018; 18:258. [PubMed: 29866059]
41. Byrne DD, Tate JP, Forde KA, Lim JK, Goetz MB, Rimland D, et al.Risk of acute liver injury after statin initiation by human immunodeficiency virus and chronic hepatitis C virus infection status. Clin Infect Dis2017; 65:1542–1550. [PubMed: 29020184]
42. Feinstein MJ, Achenbach CJ, Stone NJ, Lloyd-Jones DM. A systematic review of the usefulness of statin therapy in HIV-infected patients. Am J Cardiol2015; 115:1760–1766. [PubMed: 25907504]
43. Gilbert JM, Fitch KV, Grinspoon SK. HIV-Related cardiovascular disease, statins, and the REPRIEVE Trial. Top Antivir Med2015; 23:146–149. [PubMed: 26713505]
44. Proia KK, Thota AB, Njie GJ, Finnie RK, Hopkins DP, Mukhtar Q, et al., Community Preventive Services Task Force. Team-based care and improved blood pressure control: a community guide systematic review. Am J Prevent Med2014; 47:86–99.
45. Maina G, Mill J, Chaw-Kant J, Caine V. A systematic review of best practices in HIV care. J HIV AIDS Soc Serv2016; 15:114–126. [PubMed: 27152102]
46. Ghehi C, Gabillard D, Moh R, Badje A, Kouame GM, Oouttara E, et al.High correlation between Framingham equations with BMI and with lipids to estimate cardiovascular risks score at baseline in HIV-infected adults in the Temprano trial, ANRS 12136 in Cote d'Ivoire. PLoS One2017; 12:e0177440. [PubMed: 28582393]
47. Sullivan LM, Massaro JM, D'Agostino RB Sr. Presentation of multivariate data for clinical use: the Framingham Study risk score functions. Stat Med2004; 23:1631–1660. [PubMed: 15122742]
48. Regan S, Meigs JB, Massaro J, D'Agostino RB, Grinspoon SK, Triant VA. Evaluation of the ACC/AHA CVD risk prediction algorithm among HIV-infected patients. In: Conference on Retroviruses and Opportunistic Infections. Seattle, WA; 2015.

AIDS. Author manuscript; available in PMC 2021 September 09.

Table 1.

Demographic and clinical characteristics and cardiovascular risk factors among US adults living with HIV – HIV Outpatient Study, 2010–2017.

Characteristics	Men	Women
Total (*N*)	2467	619
Age group (years) [*n* (%)]		
30–39	359 (14.6)	82 (13.2)
40–49	1011 (41)	264 (42.6)
50–59	819 (33.2)	212 (34.2)
60–74	278 (11.3)	61 (9.9)
Race/ethnicity [*n* (%)]		
Non-Hispanic/Latino white	1300 (52.7)	119 (19.2)
Non-Hispanic/Latino black	583 (23.6)	338 (54.6)
Other	584 (23.7)	162 (26.2)
Education [*n* (%)]		
Less than high school	192 (7.8)	185 (29.9)
High school	317 (12.8)	160 (25.8)
More than high school	1343 (54.4)	173 (27.9)
Other/unknown	615 (24.9)	101 (16.3)
$CD4^+$ T-lymphocyte cell count (cells/μl) [n (%)][a]		
0–199	249 (10.1)	75 (12.1)
200–349	396 (16.1)	122 (19.7)
350–499	463 (18.8)	109 (17.6)
At least 500	1329 (53.9)	307 (49.6)
None/missing	30 (1.2)	6 (1.0)
Median (IQR)	527 (337, 735)	500 (293, 767)
Nadir $CD4^+$ T-lymphocyte cell count (cells/μl) [*n* (%)][b]		
0–199	1158 (46.9)	299 (48.3)
200–349	634 (25.7)	166 (26.8)
350–499	409 (16.6)	81 (13.1)
At least 500	261 (10.6)	72 (11.6)
None/missing	5 (0.2)	1 (0.2)

Characteristics	Men	Women
Median (IQR)	218 (82, 364)	202.5 (59, 347)
HIV disease stage [*n* (%)]		
AIDS	1451 (58.8)	400 (64.6)
Non-AIDS	1016 (41.2)	219 (35.4)
Virally suppressed[c] [*n* (%)]		
Yes	1621 (65.7)	312 (50.4)
No	818 (33.2)	303 (48.9)
Missing	28 (1.1)	4 (0.6)
Years since HIV diagnosis [*n* (%)]		
< 5 years	467 (18.9)	137 (22.1)
5–10 years	454 (18.4)	120 (19.4)
>10 years	1546 (62.7)	362 (58.5)
Hepatitis C virus coinfection [*n* (%)]		
Yes	368 (14.9)	159 (25.7)
No	2099 (85.1)	460 (74.3)
eGFR <60 ml/min/1.73 m^2 [d]		
Yes	300 (12.2)	82 (13.2)
No	2156 (87.4)	537 (86.8)
Missing	11 (0.4)	0 (0)
Risk factors used to calculate heart age		
Age, years, mean (SD)	49.3 (8.3)	49.1 (8.1)
Total cholesterol (mg/dl), mean (SD)	178.3 (41.6)	180.4 (41.8)
HDL cholesterol (mg/dl), mean (SD)	45.3 (16.1)	51.8 (17.5)
Systolic blood pressure (mmHg), mean (SD)	126.3 (15.9)	123.7 (17.8)
BMI (kg/m^2), mean (SD)	26.7 (5.0)	29.5 (8.3)
Antihypertensive treatment [*n* (%)]	591 (24.0)	208 (33.6)
Current smoker[e] [*n* (%)]	1271 (51.5)	401 (64.8)
Diabetes [*n* (%)]	368 (14.9)	145 (23.4)
BMI (kg/m^2)[f] [*n* (%)]		
Underweight (BMI <18.5)	54 (2.2)	24 (3.9)

Characteristics	Men	Women
Normal (18.5 ≥BMI <25)	945 (38.3)	184 (29.7)
Overweight (25 ≥BMI <30)	974 (39.5)	152 (24.6)
Obese (BMI ≥30)	494 (20.0)	259 (41.8)
Cholesterol-lowering medication (statin) use[g] [*n* (%)]		
Yes	368 (14.9)	113 (18.3)
No	2099 (85.1)	506 (81.7)
Aspirin use[g] [*n* (%)]		
Yes	201 (8.1)	53 (8.6)
No	2266 (91.9)	566 (91.4)
ARV regimen used at baseline[g] [*n* (%)]		
NRTI-containing	3263 (89.7)	887 (89.9)
NNRTI-containing	1378 (37.9)	327 (33.1)
Boosted protease inhibitor-containing	1552 (42.7)	416 (42.1)
ARV exposure history unknown	99 (2.7)	31 (3.1)
Years of ARV use[h], median (IQR)		
cART[i]	7.1 (2.4, 11.7)	5.6 (1.4, 10.4)
NRTI	7.5 (2.5, 12.7)	6.0 (1.6, 11.3)
NNRTI	1.4 (0, 5.9)	0.7 (0, 3.8)
Boosted protease inhibitors	0 (0, 3.7)	0.1 (0, 3.7)

The observation period was defined as the period of time from 365 days before through 365 days after index date. ARV, antiretroviral therapy; cART, combination antiretroviral therapy; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; IQR, interquartile range; NNRTI, nonnucleoside reverse transcriptase inhibitors; NRTI, nucleoside reverse transcriptase inhibitors; PI, protease inhibitor.

[a] $CD4^+$ count on the date of the index record, or during the observation period.

[b] Nadir $CD4^+$ cell was defined as the lowest $CD4^+$ count level since enrollment in the HOPS.

[c] Virally suppressed indicates that the most recent viral load during the observation period was undetectable or 200 copies/ml or less.

[d] Most recent laboratory measurement during the observation period.

[e] Data regarding smoking status were collected at time of HOPS entry and updated through telephone audio computer-assisted self-interviewing conducted during clinical visits. Smoking status reflects report at the index visit or during the observation period.

[f] BMI [weight (kg)/height (m^2)] was computed using weight measured at the index visit and height from any visit.

[g] Any use during the observation period.

[h] Medians and IQRs include only patients for whom complete ARV history was known.

[i] cART was defined as the following regimens: any combination of three ARVs that included a PI; NNRTI; a fusion, entry or integrase inhibitor; or a CCR5 antagonist; any combination of three NRTIs that included abacavir (ABC) or tenofovir (TDF), with the exception of the following combinations: ABC with TDF combined with lamivudine and didanosine with TDF and lamivudine; two full-dose PIs; a ritonavir-boosted PI combined with either an NNRTI or fusion inhibitor; an integrase inhibitor combined with either a PI, an NNRTI, an entry inhibitor or a CCR5 antagonist.

Table 2.

Predicted heart age, excess heart age, and prevalence of at least 10 years excess heart age among US adults living with HIV – HIV Outpatient Study (HOPS), 2010–2017, $n = 3086$.

	Men ($n = 2467$)			Women ($n = 619$)		
Characteristics	**Predicted heart age[b] (years) (95% CI)**	**Excess heart age (years) (95% CI)[c]**	**Excess heart age at least 10 years[d,e] (%) (95% CI)**	**Predicted heart age[b] (years) (95% CI)**	**Excess heart age (years) (95% CI)[c]**	**Excess heart age at least 10 years[d,e] (%) (95% CI)**
Total	60.8 (60.3–61.4)	11.5 (11.1–12.0)	53.1 (51.2–55.1)	62.2 (61.0–63.4)	13.1 (12.0–14.1)	59.3 (55.4–63.1)
Age group (years)						
30–39	44.8 (43.9–45.7)	7.8 (6.9–8.8)	35.1 (30.3–40.2)	45.1 (42.4–47.8)	7.7 (4.9–10.4)	39.0 (29.1–49.9)
40–49	56.7 (56.0–57.4)	11.2 (10.5–11.8)	49.6 (46.5–52.6)	58.1 (56.3–59.8)	13.0 (11.3–14.7)	56.1 (50.0–61.9)
50–59	68.0 (67.3–68.7)	13.7 (13.0–14.4)	61.5 (58.2–64.8)	70.7 (69.1–72.3)	16.4 (14.8–18.0)	70.3 (63.8–76.0)
60–74	75.6 (74.7–76.4)	11.3 (10.4–12.2)	64.7 (59.0–70.1)	73.6 (71.2–76.0)	9.1 (6.6–11.6)	62.3 (49.6–73.5)
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001
Race/ethnicity						
Non-Hispanic/Latino white	61.2 (60.4–61.9)	11.0 (10.5–11.6)	51.5 (48.7–54.2)	62.0 (59.2–64.8)	12.6 (10.3–14.8)	60.5 (51.5–68.9)
Non-Hispanic/Latino black	60.1 (59.0–61.3)	12.4 (11.5–13.2)	57.3 (53.2–61.2)	63.3 (61.6–64.9)	14.2 (12.8–15.6)	62.1 (56.8–67.1)
Other	60.9 (59.7–62.0)	11.9 (11.0–12.7)	52.7 (48.7–56.8)	60.1 (57.5–62.6)	11.1 (9.0–13.2)	52.5 (44.8–60.0)
P value	0.0043	0.0009	0.0021	0.1896	0.1038	0.1934
Education						
Less than high school	65.1 (63.1–67.2)	13.9 (12.5–15.3)	60.9 (53.9–67.6)	62.2 (60.1–64.3)	14.0 (12.1–15.9)	62.2 (55.0–68.9)
High school	61.6 (60.2–63.1)	13.4 (12.3–14.5)	60.6 (55.1–65.8)	61.1 (58.5–63.6)	12.4 (10.3–14.5)	56.2 (48.5–63.7)
More than high school	60.7 (59.9–61.4)	10.9 (10.4–11.5)	50.4 (47.7–53.1)	62.5 (60.0–64.9)	12.9 (10.9–14.8)	60.1 (52.6–67.1)
P value	0.0007	0.0006	0.0095	0.6694	0.5828	0.5465
Cholesterol-lowering medication	(statin) use					
Yes	67.3 (66.0–68.6)	15.1 (14.0–16.1)	66.6 (61.6–71.2)	71.3 (69.2–73.3)	18.6 (16.6–20.6)	77.0 (68.3–83.8)
No	59.7 (59.1–60.3)	10.9 (10.5–11.4)	50.8 (48.6–52.9)	60.2 (58.8–61.6)	11.8 (10.7–13.0)	55.3 (51.0–59.6)
P value	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0004
Aspirin use						
Yes	69.9 (68.3–71.5)	16.1 (14.7–17.6)	73.1 (66.6–78.8)	72.4 (69.8–75.1)	19.4 (16.7–22.1)	83.0 (70.5–90.9)
No	60.0 (59.5–60.6)	11.1 (10.7–11.6)	51.4 (49.3–53.4)	61.2 (59.9–62.6)	12.5 (11.4–13.6)	57.1 (53.0–61.1)
P value	<0.0001	<0.0001	<0.0001	0.0004	0.0017	0.0040

Characteristics	Men (*n* = 2467)			Women (*n* = 619)		
	Predicted heart age[b] (years) (95% CI)	Excess heart age (years) (95% CI)[c]	Excess heart age at least 10 years[d,e] (%) (95% CI)	Predicted heart age[b] (years) (95% CI)	Excess heart age (years) (95% CI)[c]	Excess heart age at least 10 years[d,e] (%) (95% CI)
Hepatitis C virus co-infection						
Yes	64.9 (63.6–66.2)	13.3 (12.3–14.3)	60.9 (55.8–65.7)	64.3 (61.8,66.7)	13.2 (11.3,15.2)	64.8 (57.1,71.8)
No	60.1 (59.5–60.7)	11.2 (10.8–11.7)	51.8 (49.6–53.9)	61.5 (60.0,62.9)	13.0 (11.8,14.2)	57.4 (52.8,61.8)
P value	0.0063	0.0230	0.0684	0.7524	0.4523	0.4242
eGFR <60 ml per min per 1.73 m^2						
Yes	66.4 (64.9–67.9)	12.4 (11.3–13.6)	59.7 (54.0–65.1)	69.0 (66.1–71.9)	15.3 (12.7–17.8)	71.9 (61.3–80.6)
No	60.1 (59.5–60.6)	11.4 (11.0–11.8)	52.1 (50.0–54.2)	61.2 (59.8–62.5)	12.7 (11.6–13.9)	57.4 (53.1–61.5)
P value	0.0312	0.1614	0.2471	0.0151	0.1135	0.0488
$CD4^+$ T-lymphocyte cell count (cells/μl)						
0–199	59.9 (58.2–61.6)	11.4 (10.2–12.7)	55.8 (49.6–61.9)	60.0 (56.6–63.3)	13.2 (10.3–16.0)	57.3 (46.0–68.0)
200–349	62.2 (60.8–63.6)	11.9 (10.9–13.0)	56.1 (51.1–60.9)	61.2 (58.3–64.2)	11.8 (9.5–14.1)	59.0 (50.1–67.4)
350–499	60.3 (59.0–61.6)	10.8 (9.8–11.7)	49.2 (44.7–53.8)	61.8 (58.8–64.7)	12.3 (10.0–14.7)	54.1 (44.7–63.2)
At least 500	60.8 (60.1–61.6)	11.7 (11.2–12.3)	53.3 (50.6–55.9)	63.4 (61.7–65.2)	14.1 (12.6–15.6)	62.9 (57.3–68.1)
P value	0.2103	0.2282	0.2387	0.0901	0.0621	0.6883
Nadir $CD4^+$ T-lymphocyte cell count (cells/μl)[f]						
0–199	62.0 (61.2–62.8)	12.0 (11.4–12.5)	56.0 (53.1–58.8)	63.0 (61.2–64.7)	13.7 (12.3–15.2)	61.9 (56.2–67.2)
200–349	60.2 (59.2–61.3)	11.1 (10.3–11.9)	50.5 (46.6–54.4)	60.2 (57.6–62.7)	11.4 (9.4–13.4)	53.0 (45.4–60.5)
350–499	60.1 (58.8–61.5)	11.2 (10.2–12.2)	51.3 (46.5–56.2)	61.8 (58.8–64.7)	12.3 (10.0–14.7)	56.8 (45.9–67.1)
At least 500	58.2 (56.5–59.9)	11.2 (9.9–12.4)	49.8 (43.8–55.8)	64.7 (61.2–68.3)	15.0 (12.1–17.9)	66.7 (55.1–76.6)
P value	0.6332	0.7528	0.5588	0.1669	0.2346	0.3187
HIV disease stage						
AIDS	62.3 (61.6–63.0)	12.1 (11.6–12.7)	56.1 (53.5–58.6)	63.0 (61.4–64.5)	13.3 (12.1–14.6)	61.0 (56.1–65.7)
Non-AIDS	58.8 (57.9–59.6)	10.7 (10.1–11.4)	48.9 (45.9–52.0)	60.8 (58.7–62.9)	12.6 (10.9–14.3)	56.2 (49.5–62.6)
P value	0.0070	0.0392	0.0374	0.7612	0.7207	0.4727
Virally suppressed[g]						
Yes	61.1 (60.4–61.8)	11.3 (10.8–11.8)	52.4 (49.9–54.8)	63.1 (61.3–64.9)	13.2 (11.7–14.7)	60.6 (55.0–65.9)
No	60.3 (59.3–61.2)	11.9 (11.2–12.6)	54.5 (51.1–57.9)	61.4 (59.7–63.1)	13.1 (11.6–14.5)	58.4 (52.8–63.8)
P value	0.3487	0.2658	0.4242	0.0734	0.1051	0.2657

AIDS. Author manuscript; available in PMC 2021 September 09.

Characteristics	Men (*n* = 2467)			Women (*n* = 619)		
	Predicted heart age[b] (years) (95% CI)	Excess heart age (years) (95% CI)[c]	Excess heart age at least 10 years[d,e] (%) (95% CI)	Predicted heart age[b] (years) (95% CI)	Excess heart age (years) (95% CI)[c]	Excess heart age at least 10 years[d,e] (%) (95% CI)
Years since HIV diagnosis, *n* (%)						
<5 years	56.2 (55.0–57.4)	10.8 (9.8–11.7)	48.2 (43.7–52.7)	60.2 (57.4–63.0)	12.3 (10.1–14.6)	51.1 (42.8–59.4)
5–10 years	57.2 (55.9–58.4)	10.8 (9.9–11.8)	48.2 (43.7–52.8)	60.0 (57.1–62.9)	12.0 (9.6–14.4)	56.7 (47.7–65.2)
>10 years	63.3 (62.7–64.0)	12.0 (11.5–12.5)	56.1 (53.6–58.5)	63.7 (62.1,65.3)	13.7 (12.4–15.0)	63.3 (58.2–68.1)
P value	0.1692	0.9250	0.5623	0.5278	0.6300	0.1146

CI, confidence intervals.

[a]The cholesterol-based heart age model includes the following measures: age, total cholesterol, high-density lipoprotein cholesterol, mean SBP, antihypertensive medication use, smoking status, and diabetes status.

[b]Predicted heart age is adjusted for age and race/ethnicity except in the age strata where it is adjusted only for race/ethnicity and in the race/ethnicity strata where it is adjusted only for age. *P* values were found by analysis of variance test and similarly adjusted.

[c]Excess heart age was calculated as predicted heart age minus chronological age. *P* value were found by analysis of variance test and adjusted for age and race/ethnicity.

[d]The proportion of participants with heart age that exceeded their chronological age by at least 10 years were calculated based on the calculated excess heart age of each individual. *P* values were found by logistic regression and adjusted for age and race/ethnicity.

[e]Estimated 95% confidence intervals (CIs) for prevalence estimates were calculated by transforming corresponding logit estimates from logistic regression into probability bounds.

[f]Nadir $CD4^+$ cell was defined as the lowest $CD4^+$ count level since inclusion in the HOPS.

[g]Virally suppressed indicates that the most recent viral load during the observation period (from 365 days before through 365 days after the index date) was undetectable or 200 copies/ml or less.