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Life Course History of Physical and Sexual Abuse is Associated with Cardiovascular Disease Risk Among Women Living with and without HIV

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RUNNING HEAD: Life course abuse history, CVD risk, and HIV

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ABSTRACT

Objective. Sexual and physical abuse predict cardiovascular disease (CVD) among women in the general population. Women living with HIV (WLWH) report more abuse and have higher CVD risk compared to other women, yet associations between abuse history and CVD have not been considered among WLWH. This study fills this gap, and describes possible pathways linking abuse to CVD risk among WLWH and women living without HIV (WLWOH).

Methods. Using 25 years of data from the Women's Interagency HIV Study (n=2734; WLWH n=1963; WLWOH n=771), we used longitudinal generalized estimating equations to test associations between sexual (SA) and physical abuse (PA) with CVD risk. Framingham (FRS-H) and

the American College of Cardiology/American Heart Association-Pooled Cohort Equation (ACC/AHA-PCE) scores were examined. Analyses were stratified by HIV-serostatus.

Results. Among WLWH, childhood SA was associated with higher CVD risk ($\beta_{FRS\text{-}H}$=1.25, SE=1.08, p=0.005; $\beta_{ACC/AHA\text{-}PCE}$=1.14, SE=1.07, p=0.04) compared to no abuse. Adulthood SA was associated with higher CVD risk for WLWH ($\beta_{FRS\text{-}H}$=1.39, SE=1.08, p<0.0001) and WLWOH ($\beta_{FRS\text{-}H}$=1.58, SE=1.14, p=0.0006). Childhood PA was not associated with CVD risk for either group. Adulthood PA was associated with CVD risk for WLWH ($\beta_{FRS\text{-}H}$=1.44, SE=1.07; p<0.0001, $\beta_{ACC/AHA\text{-}PCE}$=1.18, SE=1.06, p=0.002) and WLWOH ($\beta_{FRS\text{-}H}$=1.68, SE=1.12, p<0.0001; $\beta_{ACC/AHA\text{-}PCE}$=1.24, SE=1.11, p=0.03). Several pathway factors were significant, including depression, smoking, and hepatitis-C infection.

Conclusions. Life course abuse may increase CVD risk among WLWH and women at high risk of acquiring HIV. Some co-morbidities help explain the associations. Assessing abuse experiences in clinical encounters may help contextualize cardiovascular risk among this vulnerable population and inform intervention.

Non-standard Abbreviations and Acronyms: Adverse Childhood Experiences (ACEs), Women Living with HIV (WLWH), Women Living without HIV (WLWOH), Framingham Risk Score for Hard Events (FRS-H), American College of Cardiology/American Heart Association-Pooled Cohort Equation (ACC/AHA-PCE)

INTRODUCTION

Adverse childhood experiences (ACEs) are traumatic and stressful events occurring before age 18 years, including physical and sexual abuse, neglect, and household dysfunction[1,2]. ACEs are common; 61% of adults report at least one, and 16% report four or more ACEs[3,4]. ACEs are associated with a many poor physical, behavioral, and mental health outcomes across the life course[1,5], with sexual and physical abuse (the most severe ACEs) yielding the strongest

associations with later life outcomes[3,4,6]. Increasingly, providers are screening for ACEs in pediatric and adult primary care settings[7,8], with California recently mandating insurance coverage for ACE screening statewide[9]. Thus, while ACEs are an important concern for children, ACEs also have far-reaching impacts for health and clinical practice for adults.

Studies show consistent associations between ACEs and adulthood cardiovascular disease (CVD) in the general population[1,10–12]. The landmark CDC Adverse Childhood Experiences Study (n=13,494) found those with ≥4 ACEs experienced 2-fold increased risk of stroke and ischemic heart disease compared to those with no ACEs[1]. Dose-response associations have been consistently observed with cardiometabolic risks, including hypertension, dyslipidemia, obesity, and diabetes[2,10]. Despite this evidence, researchers have not considered the ACEs and CVD association among people living with HIV (PLWH). This is a key omission in the literature because PLWH and those at risk for acquiring HIV, including sexual and gender minority populations, tend to experience more ACEs than people without HIV[3,13–16]. Moreover, people with ACEs are more likely to experience intimate partner violence and other abuses later in life[17], particularly women living with HIV[18,19]. In addition, with increased utilization of effective antiretroviral therapy, AIDS mortality has decreased and survival times have increased among PLWH[20]. Yet with this prolonged survival, PLHW experience a 2-fold increased risk of CVD compared to the general population[21–24], and CVD emerges earlier in life and is a leading cause of non-AIDS mortality[25–27]. Given that PLWH are more likely to experience adversity across the life course and also have a high degree of CVD morbidity, it is plausible that abuse may contribute to cardiovascular risk among PLWH. This possibility has not been tested.

The pathways linking abuse experience to CVD risk among the general population include structural, psychosocial, behavioral, and physiologic factors[10]. While similar pathways are likely at play for PLWH, there may also be important differences given the underlying inflammatory state associated with HIV[28], adverse cardiovascular effects of historical antiretroviral treatment[29], and

higher prevalence of health risk behaviors and co-morbidities like smoking[30], injection drug use, and hepatitis-C virus (HCV) infection[31]. Thus, the identification of pathways linking abuse with CVD among PLWH is warranted and may reveal novel opportunities for intervention.

A recent Scientific Statement by the American Heart Association (AHA)[10] and expert consensus from the National Institutes of Health/Heart Lung and Blood Institute (NIH/NHLBI)[6] indicated that while the association between ACEs and CVD has been consistent across studies in the general population, gaps remain, including characterizing the association among vulnerable populations and describing pathways through which ACEs may influence adulthood CVD. Therefore, we examined the association between life course history of sexual and physical abuse with CVD risk using 25 years of prospectively collected data among women living with HIV (WLWH) and socio-demographically similar women living without HIV (WLWOH) but at high risk for acquiring HIV. We also examined potential pathways through which abuse may contribute to CVD risk in this vulnerable population.

METHODS

Study Population

The Women's Interagency HIV Study (WIHS) was a longstanding multi-site, prospective cohort of United States women living with and without HIV. Women were recruited at 10 sites over 4 time periods starting in 1994, with follow up through 2019. WIHS methods and cohort characteristics have been described elsewhere[32]. Briefly, WLWH were eligible to participate if they were HIV-seropositive, assigned female sex at birth, and did not acquire HIV perinatally. WLWOH were eligible if she or her partner met at least one of the following criteria within 5 years prior to enrollment: diagnosis of >1 sexually transmitted infection, unprotected sex with $\geq$6 individuals, having sex for money, drugs, or shelter, sex with an HIV-positive individual, injection drug use, unprescribed drug use (crack, cocaine, heroin, methamphetamine). Information on HIV treatment during the study period was repeatedly assessed. At the last study visit included in the

present analysis, 85.5% were receiving antiretroviral treatment, with combination antiretroviral therapy integrase inhibitors (39%), protease inhibitors (24.7%), and nucleoside/nucleotide analogue reverse transcriptase inhibitors (18.2%) being the most prevalent. Data were collected using structured in-person interviews and standardized physical and laboratory assessments; study visits occurred every six months. Beginning in 2019, follow up is continuing as part of the Multicenter AIDS Cohort Study/WIHS Combined Cohort Study (MWCCS)[33].

HIV seroconversions (n=21) and participants missing abuse and outcome information were excluded, resulting in n=2734 for the present analysis (n=771 WLWOH; n=1963 WLWH). Participants had a median of 23 study visits (IQR: 12-31; WLWOH: median 23, IQR: 13-31; WLWH: median 23, IQR: 12-31). The median date of the abuse history data collected at enrollment was 11/07/2006 (IQR: 05/05/1995-02/28/2007) for WLWH and 11/27/2006 (IQR: 03/13/1995-03/13/2007) for WLWOH. Outcomes were ascertained through 9/30/2019. Institutional review boards at the clinical research centers approved protocols, and participants provided written informed consent. This sub-study was additionally approved by the University at Albany.

Measures

Cardiovascular Risk Scores. We calculated the Framingham Risk Score for hard events (FRS-H), which indicates the 10-year risk for myocardial infarction and coronary death[34–36]; and the American College of Cardiology/American Heart Association-Pooled Cohort Equations for atherosclerotic disease (ACC/AHA-PCE) which indicates the 10-year risk of hard atherosclerotic events, defined as coronary death, non-fatal myocardial infarction, and fatal or non-fatal stroke[37]. Scores were calculated using age, hypertension treatment (yes/no), smoking status (yes/no); measured systolic blood pressure (mmHg), total and HDL cholesterol (Roche Diagnostics Corporation, Indianapolis, IN). The ACC/AHA-PCE additionally included race (Black/African-American vs. other) and diabetes (fasting glucose ≥126 mg/dl, hemoglobin A1c ≥6.5%, self-report of diabetes, or taking diabetes medication at the visit). Risk scores were calculated for established valid

age ranges (FRS-H: 30-79 years[34]; ACC/AHA-PCE=40-75 years[37]). Risk scores were natural log transformed due to skewed distributions.

Lifetime history of sexual and physical abuse. At WIHS enrollment, participants answered the following questions on abuse history: "*At any time in your life, has anyone ever pressured or forced you to have sexual contact? By sexual contact I mean them touching your sexual parts, you touching their sexual parts, or sexual intercourse.*"; and "*Have you ever experienced serious physical violence (physical harm by another person)? By that I mean were you ever hurt by a person using an object or were you ever slapped, hit, punched, kicked?*" For "yes" responses to either item, follow-up questions determined the age when the abuse first occurred. Two three-category variables were created reflecting whether the abuse occurred in childhood (before 18 years), in adulthood, or the abuse did not occur. Physical abuse (PA) and sexual abuse (SA) were examined separately in analysis.

Covariates. Potential confounders included study site, enrollment wave, education at enrollment (high school or less versus more than high school), and among WLWH, CD4 T cell count/uL, use of antiretroviral therapy, and HIV viral load below the lower limit of quantification (LLQ). Adjusted models for FRS-H additionally included race. Age is a component of the CVD risk outcome variables and was therefore not controlled for in analysis.

Pathway variables. We considered several variables that could possibly link abuse history to CVD events and atherosclerotic disease[10]: depressive symptoms as measured by the Center for Epidemiologic Studies Depression Scale[38], body mass index (BMI; kg/m^2), alcohol use (number of drinks per week), injection drug use (yes/no), cholesterol medication use (yes/no), hepatitis-C virus (HCV) serostatus, and the component parts of the CVD risk scores (total cholesterol, HDL, systolic blood pressure (SBP), hypertension medication use, diabetes, cigarette smoking).

Statistical Analysis

We defined the baseline visit for each participant as the first ascertainment of the CVD risk scores. Given the different age ranges applicable for the outcome measures, baseline assessments for FRS-H and AHA/ACC-PCE could occur at different visits. Therefore, we examined the distribution of study variables according to abuse history type within strata of HIV separately for the baseline FRS-H and AHA/ACC-PCE visit. Also, we tested the baseline cross-sectional associations between abuse history, CVD risk, and other study variables within HIV strata using χ^2-square and ANOVA tests for categorical and continuous variables respectively. Next, longitudinal associations between abuse history with CVD risk were estimated using repeated measures linear regression models with generalized estimating equations (GEE), with exchangeable covariance structures. GEE is an extension of generalized linear models applicable to longitudinal data as it can accommodate missing observations and account for correlated observations within participants, and models the average (marginal) response over time[39]. Unadjusted and adjusted GEE models were fit sequentially. Potential pathways were assessed in two ways. First, pathway variables that were not part of the risk scores were added to the adjusted models. We interpreted attenuated coefficients with the addition of pathway variables to models by approximately 10% and change in significance thresholds to suggest possible mediation[40,41]. Second, we examined longitudinal associations between abuse history with component parts of the CVD risk scores and other possible pathways factors as separate outcomes with GEE linear and logistic regressions. All models were stratified by HIV serostatus. Adjusted models included both time-varying (e.g., CD4 count) and time-invariant (e.g., study site) covariates. The regression parameter estimates for CVD risk were back-transformed from the natural log scale and can be interpreted as percent change in 10-year CVD risk according to abuse exposure. Statistical significance was defined as two-tailed $\alpha<0.05$. Analyses were conducted using SAS 9.4 (Cary, NC).

RESULTS

Sexual Abuse History and CVD Risk at Baseline

Table 1 lists participant characteristics according to SA history and HIV serostatus. There were no differences in baseline CVD risk according to SA among WLWH and WLWOH. Among WLWH, the prevalence of childhood and adulthood SA was 18% and 20% respectively, and the average baseline FRS-H was 1.61% (SD=2.08) and ACC/AHA-PCE was 5.21% (SD=8.05). Among WLWOH, the prevalence of childhood and adulthood SA was 19% and 20% respectively, and the average initial FRS-H was 1.95% (SD=3.15) and ACC/AHA-PCE was 3.64% (SD=7.22). There was a small degree of overlap for sexual and physical abuse history: 4.69% of WLWH reported both SA and PA in childhood, and 14.06% reported both forms of abuse in adulthood. For WLWOH, 4.15% reported both SA and PA occurring in childhood and 14.92% reported both in adulthood. Some significant differences according to SA history were noted at baseline, including race, education, depressive symptoms, smoking, HCV, injection drug use and antiretroviral use among WLWH. A high proportion of WLWH had detectable viral load across SA groups at the baseline visit (67-70%). Those with child SA history had the lowest antiretroviral use rates (p=0.04). Among WLWOH, significant baseline differences in age at first FRS-H assessment, race, depressive symptoms, injection drug use, and HCV were also observed. At the last study visit for WLWH, the prevalence of detectable viral load was 35.8%.

Physical Abuse History and CVD Risk at Baseline

Table 2 lists participant characteristics according to PA history and HIV serostatus. Among WLWH, the prevalence of childhood and adulthood PA was 10.55% and 41.77% respectively. There were no differences in baseline CVD risk according to PA history for WLWH. Among WLWOH, the prevalence of childhood and adulthood PA was 10.12% and 45.01% respectively. There were significant baseline differences in FRS-H for WLWH, with the childhood PA group having the lowest (Mean=1.51, SD=2.76) and the adulthood group having the highest FRS-H scores (Mean=1.71, SD=2.74). Some differences according to PA history at baseline were also noted for WLWH, including age at first AHA/ACC-PCE assessment, race, depressive symptoms, smoking,

injection drug use, HCV, and HIV viral load below the LLQ. A high proportion of WLWH had detectable viral load across PA groups at the baseline visit (65.17%-70.14%). Those with adult PA history had the lowest antiretroviral use rates (p=0.02). Among WLWOH, baseline differences were evident for age at first FRS-H assessment, total cholesterol, blood pressure, BMI, depressive symptoms, injection drug use, and HCV.

Supplemental Tables 1–2, http://links.lww.com/QAD/D89 list participant characteristics according to abuse history and HIV status at the baseline AHA/ACC-PCC visit. Results were similar to the characteristics described for FRS-H.

Associations Between Life Course Sexual and Physical Abuse History and CVD risk

Table 3 shows the longitudinal associations between SA and PA and CVD risk. Among WLWH, childhood SA was significantly associated with higher FRS-H (β=1.25, SE=1.08, p=0.005) and ACC/AHA-PCE (β=1.14, SE=1.07, p=0.04), adjusted for covariates. Associations were attenuated for FRS-H (β=1.16, SE=1.08, p=0.06; percent change=7.2%) and ACC/AHA-PCE (β=1.08, SE=1.06, p=0.21; percent change=5.3%) when adding pathway variables to the models, suggesting that behavioral and clinical factors may help explain the associations. Also among WLWH, adulthood SA was positively associated with FRS-H (β=1.39, SE=1.08, p<0.0001), but not ACC/AHA-PCE (β=1.11, SE=1.07, p=0.10) in covariate adjusted models. Among WLWOH, there was no significant association between childhood SA and either measure of CVD risk. Adulthood SA was positively associated with FRS-H (β=1.58, SE=1.14, p=0.0006) but not ACC/AHA-PCE (β=1.21, SE=1.12, p=0.10) in adjusted analyses for WLWOH.

There were no significant associations between childhood PA and CVD risk among WLWH or WLWOH (Table 3). For both WLWH and WLWOH, there was a positive association between adulthood PA and FRS-H (WLWH: β=1.44, SE=1.07, p<0.0001; WLWOH: β=1.68, SE=1.12, p<0.0001) and ACC/AHA-PCE (WLWH β=1.18, SE=1.06, p=0.002; WLWOH: β=1.24, SE=1.11, p=0.03) in adjusted models. Parameter estimates were attenuated in pathways models but remained

significant for both groups except for ACC/AHA-PCE among WLWOH. Among WLWOH, percent change in parameter estimates from covariate adjusted to pathways models was 15% and 11% for adulthood PA with FRS-H and ACC/AHA-PCE assessed CVD risk respectively.

Pathway Factors by Sexual Abuse History

Table 4 shows longitudinal associations between SA and possible pathway variables. Among WLWH, childhood SA was associated with more depressive symptoms (β=3.54, SE=0.59, p<0.0001), cholesterol medication use (OR=1.74, 95%CI:1.18, 2.57), smoking (OR=1.71, 95%CI:1.35, 2.16), and HCV infection (OR=1.54, 95%CI:1.16, 2.05). Also, among WLWH, adulthood SA was associated with depressive symptoms (β=3.57, SE=0.54, p<0.0001), smoking (OR=1.64, 95%CI:1.31, 2.05), and HCV (OR=2.03, 95%CI:1.55, 2.66) compared to those with no abuse history. Among WLWOH, childhood (β =4.28, SE=0.92, p<0.0001) and adulthood (β =5.78, SE=0.84, p<0.0001) SA were each positively associated with higher depression scores compared to those with no abuse. Childhood SA was associated with systolic blood pressure (β =-2.66, SE=1.30, p=0.04) and alcohol use (β=1.72, SE=0.85, p=0.04). Adulthood SA was also associated with HCV (OR=2.19, 95%CI:1.36, 3.53).

Pathway Factors by Physical Abuse History

Table 5 shows the associations between PA and possible pathway variables. Among WLWH, childhood PA was associated with depressive symptoms (β=4.64, SE=0.74, p<0.0001), alcohol use (β=1.11, SE=0.46, p=0.02), smoking (OR=2.04, 95%CI:1.51, 2.74) and HCV (OR=1.92, 95%CI:1.32, 2.78) compared to WLWH with no abuse history. Also, among WLWH, adulthood PA was associated with systolic blood pressure (β=-1.40, SE=0.62, p=0.02), depressive symptoms (β=3.84, SE=0.44, p<0.0001), alcohol use (β=1.33, SE=0.31, p<0.0001), smoking (OR=1.91, 95%CI:1.58, 2.31), HCV (OR=2.14, 95%CI:1.68, 2.72), and IDU (OR=2.00, 95%CI: 1.06, 3.77). Among WLWOH, child PA was associated with BMI (β=2.59, SE=1.18, p=0.03), and depressive symptoms (β=5.85, SE=1.18, p<0.0001) compared to those with no abuse history. Also, among WLWOH, adulthood PA was positively associated with BMI (β=1.86, SE=0.63, p=0.003),

depressive symptoms (β=5.19, SE=0.66, p<0.0001), alcohol use (β=1.49, SE=0.73, p=0.04), smoking (OR=1.80, 95%CI:1.32, 2.45), HCV (OR=2.20, 95%CI:1.41, 3.44), and IDU (OR=3.58, 95%CI:1.30, 9.82).

DISCUSSION

Using 25 years of prospective data, we found that experiencing childhood SA, one of the most severe ACEs, was associated with higher 10-year risk of hard CVD events among WLWH. Several behavioral and clinical factors helped explain the association. Experiences of SA and PA in adulthood were associated with increased CVD risk among WLWH and women at high risk of acquiring HIV. These findings are noteworthy as they indicate likelihood of hard CVD events, including myocardial infarction, stroke, and cardiovascular death. WLWH and women at risk of acquiring HIV experience many abuses over the life course. This study shows the cardiovascular impact of such abuses and addresses a key omission articulated by the AHA and NIH/NHLBI[6,10] by examining life course adversity and CVD risk in this vulnerable population.

Childhood SA was positively associated with CVD risk among WLWH. This is consistent with the general population patterns where childhood SA predicts later life CVD, often working through behavioral, physiologic, and psychological mechanisms[42]. Several pathway factors that were associated with child SA among WLWH, including depression, smoking, and HCV. While depression and smoking as pathways is consistent with the general population evidence[10,42], our study shows HCV infection could be a novel pathway linking ACEs and CVD risk for WLWH. HCV is prevalent among PLWH[43], and can affect cholesterol metabolism among PLWH[44] and those without HIV[45]; HCV also predicts CVD events among PLWH[27,43]. From a life course perspective[46,47], these findings suggest that childhood SA may lead to depression and smoking, as well as the uptake of risky sexual behavior and injection drug use, and consequent HIV and HCV infection, which may cumulatively influence CVD risk.

For WLWH and WLWOH, experiences of adulthood SA and PA were strongly associated with higher FRS-H CVD risk. Our study considered the age at which the abuse first occurred. Therefore, those with adulthood abuse did not also experience childhood abuse. Adulthood abuse, perhaps attributable in part to intimate partner violence which is prevalent among WLWH and those at risk for HIV infection[18,19], might be relevant. For pathways, we observed significant associations between adult abuse with depression, smoking, and HCV, as well as alcohol use and IDU for adult PA abuse. However, the association between adulthood abuse with CVD risk was largely maintained when controlling for pathways factors, suggesting behaviors and comorbidities explain some of the variation in CVD risk but not all.

It was surprising that childhood SA was not associated with CVD risk among seronegative women at risk of acquiring HIV, and that null findings were observed for childhood PA among all participants. Low prevalence of childhood PA (10%) and small sample size for childhood SA among WLWOH (n=148) could have constrained power to detect associations. These groups did, however, exhibit higher levels of behavioral and clinical risks over time (e.g., smoking, HCV), suggesting that it may be possible to detect risk in larger samples. Also, while the pattern of associations between SA history and ACC/AHA-PCE CVD risk were similar to FRS-H, the associations were less robust. This could be due to the differences between the CVD risk algorithms. Compared to FRS-H, ACC/AHA-PCE predicts more and different CVD endpoints, incorporates race and diabetes as component parts, and applies to an older population.

This study has some limitations. We used retrospective self-report of abuse which due to stigma and recall might contribute to misclassification of exposure and underestimated associations. Also, the CVD scores were developed for the general population and may underestimate risk among WLWH[48,49]. We examined these scores as they are common in clinical practice and allowed for comparisons between WLWH and WLWOH. While some recent work finds ACC/AHA-PCE to be a valid tool to predict CVD risk for PLWH[24,50], we acknowledge that risk scores derived for PLWH

might yield different associations with abuse history. Also, we did not conduct formal mediation tests and acknowledge that an alternative explanation for the parameter estimate changes could reflect confounding control. This study has strengths, including capitalizing on a large well-characterized longitudinal sample of women and the use of standardized CVD risk prediction tools commonly employed in clinical practice.

There are several future directions for research. First, CVD risk scores do not confirm diagnoses or describe disease progression. Future work should consider abuse history in association with major adverse cardiovascular events (MACEs) and carotid artery plaque progression among WLWH. Additionally, the pathways analysis provides a first look at possible mechanisms for abuse history and CVD among WLWH and WLWOH. Future work should conduct formal mediation analyses such as structural equation modelling[51] or effect decomposition in causal mediation[52] including with longitudinal data[53], and also consider potential reverse causation (e.g., depression, IDU, and HCV can give rise to abuse and HIV infection). Mediation analyses could also explore education attainment as mechanism. Finally, future work should study the accumulation and duration of childhood and adulthood abuse in association with CVD risk for WLWH, and associations between abuse history and CVD association among HIV-seropositive men.

Assessing life course abuse experiences in clinical encounters may help contextualize cardiovascular risk among this vulnerable population and inform intervention. The prevention and management of CVD among PLWH tends to focus on proximal risks, including lifestyle factors and medication therapy[27]. While critically important, this study additionally shows that life course abuse history, often originating decades prior to any manifestation of disease or lifestyle factor, can modulate CVD risk among WLWH. Moreover, this study also suggests that managing comorbidities like depression and HCV with a trauma-informed care lens for WLWH and women at high risk of acquiring HIV may help prevent and reduce CVD. As lifespans continue to improve for PLWH, clinicians and researchers alike should consider abuse history in clinical encounters and in the study of disease etiology and progression.

DATA AVAILABILITY STATEMENT

Access to individual-level data from the MACS/WIHS Combined Cohort Study Data (MWCCS) may be obtained upon review and approval of a MWCCS concept sheet. Links and instructions for online concept sheet submission are on the study website: https://statepi.jhsph.edu/mwccs/work-with-us/

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Table 1. Participant characteristics at baseline according to sexual abuse history and HIV serostatus among WIHS women

	WLWOH (n=771)				WLWH (n=1963)			
Characteristic	Child sexual abuse (n=147)	Adult sexual abuse (n=155)	No sexual abuse (n=469)	p^	Child sexual abuse (n=361)	Adult sexual abuse (n=401)	No sexual abuse (n=1201)	p^
CVD risk scores, Mean (SD) or n (%)								
FRS-H, 10-year risk %	1.79 (2.72)	2.13 (3.55)	1.94 (3.14)	0.30	1.59 (2.67)	1.80 (3.07)	1.55 (2.75)	0.35
ACC/AHA-PCE, 10-year risk %	4.83 (5.84)	5.61 (8.17)	5.94 (7.22)	0.59	4.72 (7.93)	5.15 (7.60)	5.41 (8.27)	0.19
CVD components, covariates, M (SD) or n (%)								
Age, first FRS-H assessment, years	42.33 (7.86)	44.76 (8.54)	42.78 (8.03)	0.03	43.11 (7.54)	43.26 (7.34)	42.62 (8.01)	0.31
Age, first ACC/AHA-PCE assessment, years	47.67 (5.24)	49.09 (6.43)	48.08 (5.67)	0.24	47.01 (5.57)	47.19 (5.43)	47.78 (5.60)	0.12
Total cholesterol, mg/dL	181.12 (40.24)	181.24 (37.23)	182.72 (38.17)	0.89	180.09 (40.21)	183.18 (43.44)	181.17 (42.47)	0.60
HDL cholesterol, mg/dL	54.15 (15.80)	56.04 (17.90)	55.60 (17.81)	0.65	49.87 (19.08)	48.86 (18.39)	49.67 (18.81)	0.72
Systolic blood pressure, mmHg	120.02 (15.40)	124.16 (22.69)	124.34 (21.11)	0.12	120.35 (17.75)	118.76 (15.69)	121.35 (18.36)	0.05
Body mass index, kg/m^2	32.59 (8.52)	32.71 (8.66)	31.53 (8.33)	0.28	29.86 (8.79)	29.56 (8.26)	30.27 (8.41)	0.37
Depressive symptoms, CES-D score	17.43 (14.31)	19.23 (13.54)	13.41 (12.39)	0.0003	16.43 (12.76)	16.73 (12.62)	13.71 (11.75)	0.0002
Alcohol use, drinks per week	7.30 (18.84)	5.02 (14.56)	6.47 (18.35)	0.57	5.03 (27.09)	2.42 (8.34)	3.23 (10.67)	0.05
Race, black	74 (61.16)	70 (51.47)	248 (70.25)	0.0004	188 (56.63)	220 (56.99)	720 (67.23)	<0.0001
Education, high school or less	72 (59.50)	80 (58.82)	228 (64.89)	0.39	211 (63.55)	220 (56.99)	752 (70.28)	<0.0001
Cholesterol medication use	10 (8.26)	11 (8.09)	25 (7.08)	0.88	22 (6.63)	30 (7.77)	88 (8.22)	0.64
Blood pressure medication use	28 (23.14)	46 (33.82)	91 (25.78)	0.11	88 (26.51)	112 (29.02)	297 (27.73)	0.75
Current smoker	79 (65.29)	80 (58.82)	201 (56.94)	0.27	185 (55.72)	195 (50.52)	473 (44.16)	0.0005
Diabetes	8 (6.61)	19 (13.97)	28 (10.76)	0.16	28 (8.43)	33 (8.55)	93 (8.68)	0.99
Hepatitis C virus infection	19 (15.70)	34 (25.19)	54 (15.34)	0.03	94 (28.40)	122 (31.77)	202 (18.91)	<0.0001
Injection drug use	32 (26.45)	42 (30.88)	53 (15.01)	0.0001	121 (36.45)	132 (34.20)	193 (18.04)	<0.0001
Covariates for WLWH, n (%) or mean (SD)								
HIV viral load, detectable					220 (67.90)	255 (67.28)	725 (70.39)	0.45
Antiretroviral therapy use					204 (61.45)	242 (62.69)	726 (67.79)	0.04

CD4 count, cells/uL					461.79 (314.28)	452.31 (288.12)	426.91 (291.90)	0.26

^p-value for ANOVA or χ^2 tests for continuous and categorical variables respectively. Cell entries reflect characteristics at the first FRS-H assessment unless otherwise specified.

HIV=Human immunodeficiency virus; WIHS=Women's Interagency HIV Study: WLWOH=Women living without HIV; WLWH=Women living with HIV; CVD=Cardiovascular disease; SD=Standard deviation; FRS-H=Framingham risk score for hard events; ACC/AHA-PCE=American college of cardiology/American heart association-pooled cohort equations; HDL=High-density lipoprotein; CES-D=Centers for epidemiologic studies depression scale; CD4=Cluster of differentiation 4

Table 2. Participant characteristics at baseline according to physical abuse history and HIV serostatus among WIHS women

	WLWOH (n=771)				WLWH (n=1963)			
Characteristic	Child physical abuse (n=78)	Adult physical abuse (n=347)	No physical abuse (n=346)	p^	Child physical abuse (n=207)	Adult physical abuse (n=820)	No physical abuse (n=936)	p^
CVD risk scores, Mean (SD) or n (%)								
FRS-H, 10-year risk %	1.46 (1.79)	2.24 (3.57)	1.72 (2.82)	0.08	1.51 (2.76)	1.71 (2.74)	1.54 (2.78)	0.03
ACC/AHA-PCE, 10-year risk %	5.18 (4.64)	5.92 (7.82)	5.35 (6.84)	0.73	4.99 (8.57)	4.79 (7.01)	5.73 (8.98)	0.20
CVD components, covariates, M (SD) or n (%)								
Age, first FRS-H assessment, years	41.44 (7.55)	44.12 (8.13)	42.27 (8.18)	0.01	40.85 (7.28)	43.77 (7.39)	42.42 (8.20)	<0.0001
Age, first ACC/AHA-PCE assessment, years	47.16 (5.24)	48.59 (5.97)	48.01 (5.68)	0.35	46.28 (5.51)	47.52 (5.37)	47.70 (5.76)	0.07
Total cholesterol, mg/dL	181.19 (38.89)	181.85 (37.58)	182.55 (39.02)	0.04	178.89 (40.44)	179.97 (40.68)	183.32 (44.05)	0.19
HDL cholesterol, mg/dL	49.88 (13.90)	56.03 (18.32)	55.96 (16.89)	0.05	49.44 (16.78)	49.78 (19.47)	49.34 (18.52)	0.90
Systolic blood pressure, mmHg	115.83 (16.42)	124.88 (20.61)	123.49 (20.97)	0.01	120.00 (18.18)	119.70 (16.81)	120.60 (18.43)	0.09
Body mass index, kg/m^2	32.98 (9.57)	32.94 (8.47)	30.62 (7.97)	0.004	30.19 (8.59)	29.65 (8.19)	30.37 (8.64)	0.26
Depressive symptoms, CES-D score	17.09 (14.48)	17.89 (13.78)	12.17 (12.53)	<0.0001	18.65 (13.49)	16.68 (12.78)	12.42 (10.86)	<0.0001
Alcohol use, drinks per week	2.79 (6.20)	7.60 (20.97)	5.47 (14.72)	0.09	4.27 (16.23)	3.79 (18.39)	2.81 (9.88)	0.29
Race, black	39 (66.10)	190 (62.50)	163 (65.99)	0.66	94 (51.37)	464 (59.26)	570 (69.26)	<0.0001
Education, high school or less	33 (55.93)	191 (62.83)	156 (63.16)	0.57	129 (70.49)	499 (63.81)	555 (67.44)	0.13
Cholesterol medication use	5 (8.47)	29 (9.54)	12 (4.86)	0.11	9 (4.92)	55 (7.02)	76 (9.23)	0.08
Blood pressure medication use	12 (20.34)	93 (30.59)	60 (24.29)	0.12	46 (25.14)	208 (26.56)	243 (29.93)	0.29
Current smoker	36 (61.02)	186 (61.18)	138 (55.87)	0.43	107 (58.47)	416 (53.13)	330 (40.10)	<0.0001
Diabetes	6 (10.17)	31 (10.20)	28 (11.34)	0.90	13 (7.10)	66 (8.43)	75 (9.11)	0.66
Hepatitis C virus infection	9 (15.25)	66 (21.71)	32 (29.91)	0.03	52 (28.42)	235 (30.09)	131 (16.00)	<0.0001

Injection drug use	9 (15.25)	81 (26.64)	37 (14.98)	0.002	63 (34.43)	260 (33.25)	123 (14.95)	<0.0001
Covariates for WLWH, n (%) or mean (SD)								
HIV viral load, detectable					116 (65.17)	525 (69.26)	559 (70.14)	0.43
Antiretroviral therapy use					120 (65.57)	486 (60.27)	566 (68.77)	0.02
CD4 count cells/uL					459.82 (308.18)	449.56 (294.39)	424.20 (293.61)	0.14

^p-value for ANOVA or χ^2 tests for continuous and categorical variables respectively. Cell entries reflect characteristics at the first FRS-H assessment unless otherwise specified.

HIV=Human immunodeficiency virus; WIHS=Women's Interagency HIV Study: WLWOH=Women living without HIV; WLWH=Women living with HIV; CVD=Cardiovascular disease; SD=Standard deviation; FRS-H=Framingham risk score for hard events; ACC/AHA-PCE=American college of cardiology/American heart association-pooled cohort equations; HDL=High-density lipoprotein; CES-D=Centers for epidemiologic studies depression scale; CD4=Cluster of differentiation 4.

Table 3. Repeated measures generalized estimating equations for the associations between cardiovascular risk scores with sexual and physical abuse history among WIHS women[a]

	WLWOH			WLWH		
	Unadjusted	Covariates	Pathways	Unadjusted	Covariates	Pathways
FRS-H						
Child sexual abuse	1.21 (1.15) 0.15	1.25 (1.14) 0.10	1.22 (1.14) 0.14	1.26 (1.08) 0.003	1.25 (1.08) 0.005	1.16 (1.08) 0.06
Adult sexual abuse	1.51 (1.14) 0.002	1.58 (1.14) 0.0006	1.42 (1.14) 0.008	1.34 (1.08) <0.0001	1.39 (1.08) <0.0001	1.30 (1.08) 0.0004
No sexual abuse (Reference)	--	--	--	--	--	--
Child physical abuse	1.09 (1.20) 0.62	1.12 (1.19) 0.52	1.03 (1.19) 0.85	1.12 (1.11) 0.26	1.12 (1.11) 0.27	1.01 (1.11) 0.92
Adult physical abuse	1.67 (1.12) <0.0001	1.68 (1.12) <0.0001	1.42 (1.11) 0.0004	1.41 (1.07) <0.0001	1.44 (1.07) <0.0001	1.29 (1.07) <0.0001
No physical abuse (Reference)	--	--	--	--	--	--
ACC/AHA-PCE						
Child sexual abuse	0.90 (1.13) 0.40	0.90 (1.13) 0.38	0.85 (1.12) 0.18	1.12 (1.07) 0.09	1.14 (1.07) 0.04	1.08 (1.06) 0.21
Adult sexual abuse	1.21 (1.13) 0.11	1.21 (1.12) 0.10	1.16 (1.12) 0.19	1.07 (1.07) 0.29	1.11 (1.07) 0.10	1.05 (1.07) 0.42
No sexual abuse (Reference)	--	--	--	--	--	--
Child physical abuse	0.88 (1.19) 0.44	0.88 (1.18) 0.44	0.81 (1.17) 0.18	0.95 (1.09) 0.70	1.01 (1.10) 0.94	0.96 (1.10) 0.64
Adult physical abuse	1.26 (1.11) 0.02	1.24 (1.11) 0.03	1.10 (1.10) 0.33	1.14 (1.06) 0.01	1.18 (1.06) 0.002	1.12 (1.05) 0.03
No physical abuse (Reference)	--	--	--	--	--	--

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Table 4. Repeated measures linear and logistic GEE models for the association between components of the CVD risk scores and pathway variables with sexual abuse history among WIHS women[a]#

	WLWOH		WLWH	
	β (SE) or OR	p or 95% CI	β (SE) or OR	p or 95% CI
Total cholesterol				
Child sexual abuse	2.41 (3.30)	0.47	-2.21 (1.96)	0.26
Adult sexual abuse	-2.75 (2.84)	0.33	1.80 (1.92)	0.35
Reference	--	--	--	--
HDL				
Child sexual abuse	0.05 (1.40)	0.97	-0.55 (0.94)	0.55
Adult sexual abuse	0.77 (1.50)	0.61	0.80 (0.87)	0.93
Reference	--	--	--	--
Systolic blood pressure				
Child sexual abuse	-2.66 (1.30)	0.04	-0.84 (0.80)	0.29
Adult sexual abuse	-1.33 (1.41)	0.34	-0.87 (0.76)	0.25
Reference	--	--	--	--
Body mass index				
Child sexual abuse	1.05 (0.82)	0.20	1.02 (0.54)	0.06
Adult sexual abuse	-0.26 (0.80)	0.74	-0.08 (0.46)	0.87
Reference	--	--	--	--
Depressive symptoms				
Child sexual abuse	4.28 (0.92)	<0.0001	3.54 (0.59)	<0.0001
Adult sexual abuse	5.78 (0.84)	<0.0001	3.57 (0.54)	<0.0001
Reference	--	--	--	--
Alcohol use				
Child sexual abuse	1.72 (0.85)	0.04	0.74 (0.39)	0.06
Adult sexual abuse	1.40 (0.97)	0.15	0.44 (0.38)	0.25
Reference	--	--	--	--
Blood pressure medication				
Child sexual abuse	0.86	0.53, 1.39	1.01	0.74, 1.37
Adult sexual abuse	1.43	0.96, 2.13	1.00	0.75, 1.33
Reference	--	--	--	--
Cholesterol medication				
Child sexual abuse	1.52	0.86, 2.72	1.74	1.18, 2.57
Adult sexual abuse	0.96	0.54, 1.70	1.05	0.68, 1.62
Reference	--	--	--	--
Diabetes				
Child sexual abuse	1.05	0.48, 2.31	1.50	0.93, 2.42
Adult sexual abuse	1.62	0.82, 3.22	0.84	0.50, 1.44
Reference	--	--	--	--
Smoker				
Child sexual abuse	1.38	0.94, 2.05	1.71	1.35, 2.16
Adult sexual abuse	1.38	0.94, 2.02	1.64	1.31, 2.05
Reference	--	--	--	--
HCV				
Child sexual abuse	1.06	0.55, 1.88	1.54	1.16, 2.05
Adult sexual abuse	2.19	1.36, 3.53	2.03	1.55, 2.66
Reference	--	--	--	--
IDU				
Child sexual abuse	2.38	0.74, 7.63	1.37	0.69, 2.70
Adult sexual abuse	1.20	0.37, 3.93	1.88	0.94, 3.75
Reference	--	--	--	--

All models adjusted for age, race, education, wave of enrollment, and study site. Models for WLWH are additional adjusted for antiretroviral therapy, CD4 count, and detectable viral load.

GEE=Generalized estimating equations; CVD=Cardiovascular disease; WIHS=Women's Interagency HIV Study; WLWOH=Women living without HIV; WLWH=Women living with HIV; SE=Standard error; OR=Odds ratio; p=p-value; CI=Confidence interval; HDL=high-density lipoprotein; HCV=Hepatitis-C infection; IDU=injection drug use.

Table 5. Repeated measures linear and logistic GEE models for the association between components of the CVD risk scores and pathway variables with physical abuse history among WIHS women[a]

	WLWOH		WLWH	
	β (SE) or OR	p or 95% CI	β (SE) or OR	p or 95% CI
Total cholesterol				
Child physical abuse	0.41 (4.17)	0.92	-4.85 (2.50)	0.05
Adult physical abuse	-0.47 (2.48)	0.85	-2.13 (1.62)	0.19
Reference	--	--	--	--
HDL				
Child physical abuse	-3.06 (1.64)	0.06	0.17 (1.08)	0.87
Adult physical abuse	-1.75 (1.17)	0.14	-0.003 (0.75)	0.99
Reference	--	--	--	--
Systolic blood pressure				
Child physical abuse	-3.45 (1.78)	0.05	1.22 (1.13)	0.28
Adult physical abuse	-0.67 (1.14)	0.55	-1.40 (0.62)	0.02
Reference	--	--	--	--
Body mass index				
Child physical abuse	2.59 (1.18)	0.03	1.15 (0.65)	0.08
Adult physical abuse	1.86 (0.63)	0.003	-0.03 (0.40)	0.96
Reference	--	--	--	--
Depressive symptoms				
Child physical abuse	5.85 (1.18)	<0.0001	4.64 (0.74)	<0.0001
Adult physical abuse	5.19 (0.66)	<0.0001	3.84 (0.44)	<0.0001
Reference	--	--	--	--
Alcohol use				
Child physical abuse	-0.09 (1.08)	0.93	1.11 (0.46)	0.02
Adult physical abuse	1.49 (0.73)	0.04	1.33 (0.31)	<0.0001
Reference	--	--	--	--
Blood pressure medication				
Child physical abuse	1.04	0.56, 1.91	0.89	0.58, 1.35
Adult physical abuse	1.19	0.84, 1.70	0.91	0.72, 1.15
Reference	--	--	--	--
Cholesterol medication				
Child physical abuse	1.64	0.78, 3.46	0.73	0.41, 1.29
Adult physical abuse	0.92	0.56, 1.49	0.98	0.71, 1.35
Reference	--	--	--	--
Diabetes				
Child physical abuse	1.32	0.53, 3.29	1.23	0.64, 2.37
Adult physical abuse	0.77	0.42, 1.41	1.08	0.71, 1.65
Reference	--	--	--	--
Smoker				
Child physical abuse	1.32	0.79, 2.18	2.04	1.51, 2.74
Adult physical abuse	1.80	1.32, 2.45	1.91	1.58, 2.31

Reference	--	--	--	--
HCV				
Child physical abuse	1.32	0.62, 2.95	1.92	1.32, 2.78
Adult physical abuse	2.20	1.41, 3.44	2.14	1.68, 2.72
Reference	--	--	--	--
IDU				
Child physical abuse	1.90	0.45, 7.97	1.52	0.62, 3.71
Adult physical abuse	3.58	1.30, 9.82	2.00	1.06, 3.77
Reference	--	--	--	--

All models adjusted for age, race, education, wave of enrollment, and study site. Models for WLWH are additional adjusted for antiretroviral therapy, CD4 count, and detectable viral load.

GEE=Generalized estimating equations; CVD=Cardiovascular disease; WIHS=Women's Interagency HIV Study; WLWOH=Women living without HIV; WLWH=Women living with HIV; SE=Standard error; OR=Odds ratio; p=p-value; CI=Confidence interval; HDL=high-density lipoprotein; HCV=Hepatitis-C infection; IDU=injection drug use.