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Piercing the veil of how substance use negatively impacts comorbidities in HIV

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Among people living with HIV (PLWH), eliminating HIV latent reservoir (HLR) is essential for a cure. Substance use may negatively impact HLR and is associated with worse outcomes for PLWH. We examined associations of cocaine use and the CD4⁺ T-cell HLR (HLR_{CD4}) in virally suppressed PLWH on downstream comorbidities. HLR_{CD4} was measured using CD4⁺ T-cell genomic DNA collected from 434 virally suppressed women of diverse ancestry (75% Black, 14% Hispanic, 12% White) who self-reported cocaine use (160 cocaine users, 274 non-users). Non-AIDS comorbidity (NACM) burden was computed at the index and 5-year follow-up visits, summing the occurrence of 10 clinically defined NACMs). Intact HLR_{CD4} was significantly larger in cocaine users (median [IQR]: 184 [28, 502]) compared to non-users (87, IQR:23, 262, p=0.0064). At the index visit, the median NACM was 3 [IQR: 2, 4], which did not differ by cocaine use (p>0.05). At follow-up, the median NACM increased to 4 [IQR: 2, 5]. We observed significantly greater HLR_{CD4} size associated with cocaine use (p=0.006). In the subset of 321 participants for whom HLR_{CD4} and NACM burden scores were available, a general estimating equation Poisson regression analysis found that larger intact HLR_{CD4} (p=0.002), greater age (p=0.013), and cocaine use (p=0.022) at index visit predicted greater NCAM burden at 5-year follow-up (p<0.0001), adjusting for index visit NCAM burden, Our study is the first to provide evidence that cocaine use and intact HLR_{CD4} may contribute to greater comorbid burden over time among PLWH.