

## **Reduced Mitochondrial DNA Copy Number in Persons who Inject Cocaine and Heroin**

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### **Background**

Mitochondrial DNA (mtDNA) copy number (CN) in blood is a marker of mitochondrial depletion and oxidative stress, and it has been associated with adverse outcomes. Mitochondrial abnormalities have been observed in persons with opiate addiction, and substance use may directly impact blood mitochondrial function. We evaluated the association of active heroin and cocaine use with mtDNA CN in a longitudinal cohort.

### **Methods**

We used data and samples from participants in the AIDS Linked to the IntraVenous Experience (ALIVE) cohort of current and former persons who inject drugs (PWID). mtDNA CN was measured in buffy coat using multiplexed real-time qPCR. Mixed effect linear regressions were used to compare mtDNA CN among people with and without active injecting drug use, heroin, and cocaine. Models were adjusted for HIV infection, demographics, cigarette, and alcohol use.

### **Results**

Of 999 participants followed for 7251 person-years, median age was 49.2 years; 37% reported active injecting drug use, 46% were people with HIV (51% of them were virally suppressed), 64% male, 88% Black, 58% had less than high school education. In multivariable regressions, compared to other participants, mtDNA CN was 0.14 standard deviations (SD) lower among persons who reported active injecting ( $p=0.025$ ). mtDNA CN was 0.17 SD and 0.25 SD lower among active cocaine and heroin users, respectively, compared to non-users (all  $p<0.05$ ). Consistent with prior findings, HIV infection, lower CD4 counts, and detectable HIV viral load were significantly associated with reduced mtDNA CN.

### **Conclusion**

Our data suggest mtDNA CN is reduced among persons with active injecting drug use, highlighting the need to investigate mitochondrial dysfunction and long-term outcomes in this population.