

Supplementary Data

SUPPLEMENTARY TABLE S1. PROPORTIONS OF PARTICIPANTS MEETING DEFICIT CRITERIA FOR EACH VARIABLE COMPRISING THE FRAILTY INDEX ACROSS HIV/METHAMPHETAMINE GROUPS

| <i>Frailty index variables</i> | A HIV-/MA- (n=91) | B HIV+/MA- (n=72) | C HIV+/MA+ (n=43) | p | <i>Pairwise comparisons</i> |
|--------------------------------|----------------------|----------------------|----------------------|----------------|-----------------------------|
| BMI | 65 (71%) | 48 (67%) | 31 (72%) | .76 | |
| Total cholesterol | 26 (29%) | 18 (25%) | 8 (20%) | .54 | |
| LDL | 60 (67%) | 33 (46%) | 20 (53%) | .02 | A > B |
| HDL | 16 (18%) | 21 (29%) | 16 (40%) | .02 | A < C |
| Triglycerides | 17 (19%) | 28 (38%) | 17 (43%) | <.01 | A < B, C |
| White blood cell count | 11 (12%) | 7 (8%) | 5 (12%) | .85 | |
| Hemoglobin | 13 (15%) | 16 (22%) | 7 (17%) | .46 | |
| Hepatitis C infection | 0 (0%) | 11 (15%) | 11 (26%) | <.01 | A < B < C |
| C-reactive protein | 49 (55%) | 41 (67%) | 24 (63%) | .30 | |
| AST | 16 (18%) | 21 (29%) | 14 (34%) | .08 | |
| ALT | 14 (15%) | 29 (40%) | 20 (49%) | <.01 | A < B, C |
| Alkaline phosphate | 4 (4%) | 5 (7%) | 4 (10%) | .50 | |
| Platelets | 1 (1%) | 7 (10%) | 3 (7%) | .03 | A < B, C |
| Potassium | 1 (1%) | 6 (8%) | 2 (5%) | .06 | |
| Bilirubin | 3 (3%) | 7 (10%) | 10 (24%) | <.01 | A, B < C |
| Unemployment | 26 (28%) | 48 (64%) | 34 (79%) | <.01 | A < B < C |
| Hypertension | 13 (14%) | 34 (45%) | 18 (42%) | <.01 | A < B, C |
| Diabetes | 6 (7%) | 10 (13%) | 4 (9%) | .33 | |
| Smoking | 10 (11%) | 29 (39%) | 24 (56%) | <.01 | A < B < C |
| Hyperlipidemia | 16 (17%) | 33 (44%) | 16 (37%) | <.01 | A < B, C |
| IL-6 | 46 (50%) | 28 (42%) | 17 (44%) | .60 | |
| MCP-1 | 46 (50%) | 49 (74%) | 33 (85%) | <.01 | A < B < C |
| sCD14 | 46 (50%) | 36 (55%) | 27 (69%) | .13 | |
| TNF-a | 46 (50%) | 36 (55%) | 34 (87%) | <.01 | A, B < C |
| D-dimer | 46 (50%) | 36 (55%) | 20 (51%) | .85 | |
| Current MDD | 0 (0%) | 5 (7%) | 8 (19%) | <.01 | A < B < C |
| Lifetime MDD | 19 (21%) | 34 (45%) | 28 (65%) | <.01 | A < B < C |

Values are presented as *N* (%); Groups were compared using chi-square likelihood ratio test, or Fisher's exact test when cell count was less than five; Pairwise comparisons were examined Bonferroni adjustments ($\alpha=0.05/3=0.0167$); **bold** values represent *p*-values that are significant at <0.05 .

Consistent with expectations, individuals in HIV+/MA+ and/or HIV+/MA- groups were more likely to meet deficit criteria for most (15 out of 27; 56%) variables compared to the control HIV-/MA- group. Significant stairstep patterns indicating additive effects of HIV and MA on likelihood of meeting deficit criteria were found for hepatitis C infection, unemployment, smoking, current MDD, lifetime MDD, and three inflammatory biomarkers: MCP-1 and TNF-a. While calculating the proportion of total deficits in a frailty index score is clinically useful for understanding total accumulated medical burden and vulnerability, a closer examination of individual components of the frailty index may lead to a greater understanding of specific pathophysiological mechanisms underlying the association between frailty and comorbid HIV and lifetime MA use disorder. Results from the current supplemental analysis support the role of a wide range mechanisms, including coinfections, metabolic factors, behavioral/psychiatric factors, and inflammation.

ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; HDL, high-density lipoprotein; IL-6, interleukin-6; LDL, low-density lipoprotein; MA, methamphetamine; MCP-1, monocyte chemoattractant protein 1; MDD, major depressive disorder; sCD14, soluble CD14; TNF-a, tumor necrosis factor alpha.