

# Web Material

## **Inflammation and Risk of Depression in HIV: Prospective Findings From the Multicenter AIDS Cohort Study**

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**Web Table 1.** Factor loadings showing the strength of association between EFA-identified inflammatory processes (EIPs) and individual markers of immune activation and inflammation in the full study sample (N=9,827 person visits)

Marker	Factor Loadings for EFA-identified Processes in CES-D Sample		
	EIP-1	EIP-2	EIP-3
sTNFr2	<b>0.92<sup>a</sup></b>	0.16	0.01
sIL2 $\alpha$	<b>0.81</b>	0.07	-0.02
sCD27	<b>0.81</b>	0.07	-0.11
BAFF	<b>0.63</b>	0.09	0.09
IP-10	<b>0.57</b>	0.16	0.11
sIL6r	<b>0.53</b>	-0.01	0.07
sCD14	<b>0.50</b>	0.04	0.10
sGP130	<b>0.47</b>	0.02	0.02
IL-6	0.21	<b>0.66</b>	0.00
IL-8	0.02	<b>0.66</b>	0.20
TNF- $\alpha$	0.39	<b>0.64</b>	0.02
MIP-1 $\beta$	-0.14	<b>0.55</b>	0.12
MCP-1	0.24	0.10	<b>0.81</b>
Eotaxin	-0.01	0.04	<b>0.67</b>
MCP-4	0.00	0.15	<b>0.49</b>
Variance explained, %	31	15	11
Cumulative variance	31	46	57

Abbreviations: BAFF, B-cell activating factor; sCD14, soluble CD14; sCD27, soluble CD 27; sGP130, soluble GP130; IL-6, interleukin 6; IL-8, interleukin 8; IP-10, interferon  $\gamma$ -induced protein 10; MCP-1, monocyte chemoattractant protein 1; MCP-4, monocyte chemoattractant protein 1; MIP-1, macrophage inflammatory protein 1 beta; sIL2 $\alpha$ , soluble interleukin 2 receptor  $\alpha$ ; sTNFr2, soluble TNF receptor 2; TNF, tumor necrosis factor; EIP, EFA-identified inflammatory process

<sup>a</sup> Boldface showing salient factors using criterion of factor loadings >0.4.

**Web Table 2.** Factor Score Distribution for Each EFA-identified inflammatory process (EIP)<sup>a</sup>, by HIV Serostatus using person-visits across time.

	Mean	Standard Deviation	Median	Minimum	Maximum
HIV+ person visits					
EIP-1	0.076	0.957	-0.045	-5.368	6.171
EIP-2	0.002	0.850	-0.125	-3.425	7.884
EIP-3	0.013	0.890	0.038	-15.295	3.103
HIV- person visits					
EIP-1	-0.583	0.778	-0.708	-2.574	5.138
EIP-2	-0.014	0.924	-0.138	4.350	7.075
EIP-3	-0.099	0.836	-0.077	-2.483	2.404

Abbreviations: EFA, exploratory factor analysis; EIP, EFA-identified inflammatory process; HIV, human immunodeficiency virus.

<sup>a</sup> EIP-1 was mainly characterized by sTNFr2, sIL2r $\alpha$ , sCD27, B-cell activating factor, IP-10, sIL6r, sCD14, and sGP130; Inflammatory process EIP-2, by IL-6, IL-8, TNF- $\alpha$ , and MIP-1 $\beta$ ; Inflammatory process EIP-3, by MCP-1, eotaxin and MCP-4.

**Web Table 3.** Adjusted logistic regression of depressive symptoms on categorical estimates of EFA-identified inflammatory processes (EIPs) comparing highest tertile EIP to lowest in HIV+ and HIV- participants from MACS from 1984 to 2010

EIP and Definition of Depression	Depressive symptoms, HIV+ participants		Depressive symptoms, HIV- participants	
	OR <sup>b</sup>	95% CI	OR	95% CI
<b>EIP-1</b>				
CES-D only <sup>c</sup>	1.21	1.06, 1.37	1.52	0.95, 2.43
CES-D + antidepressant use <sup>d</sup>	1.21	1.05, 1.39	1.15	0.76, 1.76
<b>EIP-2</b>				
CES-D only	1.08	0.96, 1.22	0.93	0.66, 1.29
CES-D + antidepressant use	1.12	1.00, 1.26	0.94	0.69, 1.29
<b>EIP-3</b>				
CES-D only	1.05	0.91, 1.21	1.00	0.70, 1.41
CES-D + antidepressant use	1.13	0.97, 1.31	0.94	0.68, 1.29

Abbreviations: MACS, the Multicenter AIDS Cohort Study; CES-D, Center for Epidemiologic Studies Depression Scale; OR, odds ratio; CI, confidence interval; EIP, EFA-identified inflammatory process

<sup>a</sup> Adjusted for age, black race, college education, current smoking, obesity, HCV infection, alcohol intake and cocaine use since last visit; generalized estimating equations (GEE) utilized for analyses.

<sup>b</sup> Comparison of highest EIP tertile to lowest EIP tertile; the ORs comparing the middle EIP tertile to the lowest were not statistically significant for all three EIPs.

<sup>c</sup> Clinically relevant depressive symptoms defined as CES-D >20 compared to having not depressive symptoms defined as CES-D <12.

<sup>d</sup> Clinically relevant depressive symptoms defined as CES-D >20 or having antidepressant use compared to having not depressive symptoms defined as CES-D <12 and having no antidepressant use.

**Web Table 4.** Adjusted logistic regression of depressive symptoms on continuous estimates of EFA-identified Processes (EIPs) in HIV+ participants stratified by calendar time (cART era and pre-cART era) from MACS from 1984 to 2010

EIP and Definition of Depression	Depressive symptoms, HIV+ participants			
	cART era <sup>a</sup>		pre-cART era	
	OR <sup>b</sup>	95% CI	OR	95% CI
<b>EIP-1</b>				
CES-D only <sup>c</sup>	1.09	1.02, 1.17	1.06	0.92, 1.21
CES-D + antidepressant use <sup>d</sup>	1.08	1.02, 1.14	1.26	1.12, 1.41
<b>EIP-2</b>				
CES-D only	1.02	0.96, 1.09	1.09	0.92, 1.31
CES-D + antidepressant use	1.00	0.95, 1.05	1.03	0.87, 1.20
<b>EIP-3</b>				
CES-D only	0.92	0.85, 1.00	1.04	0.89, 1.21
CES-D + antidepressant use	0.98	0.92, 1.04	1.13	0.97, 1.30

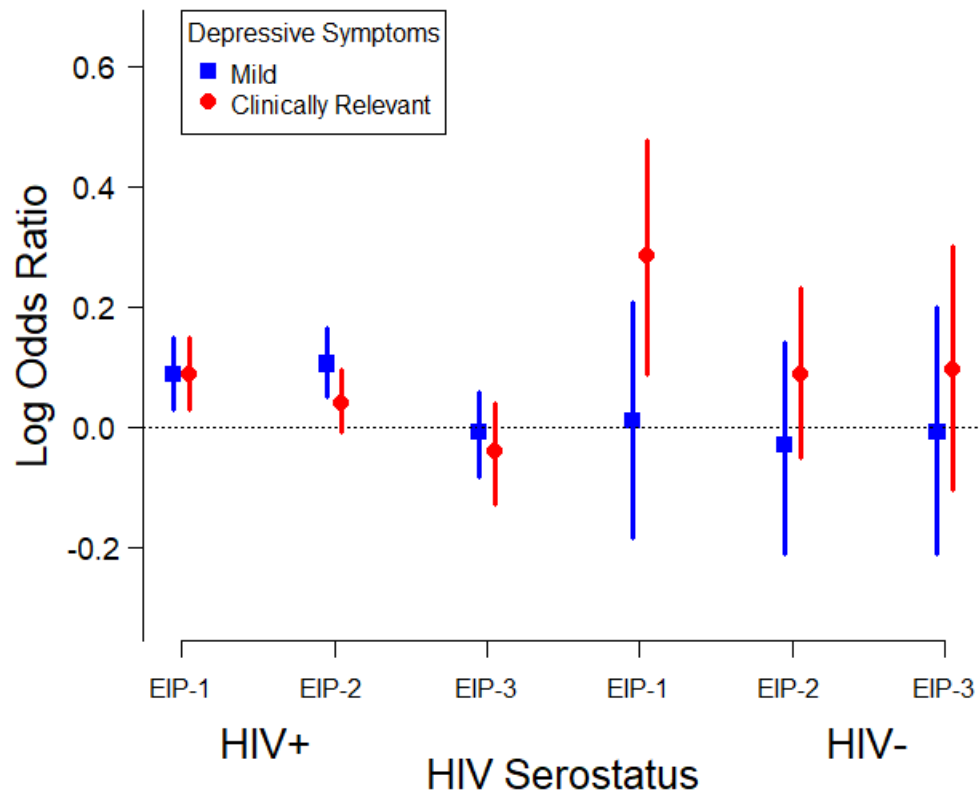
Abbreviations: MACS, the Multicenter AIDS Cohort Study; CES-D, Center for Epidemiology Study of Depression Scale; OR, odds ratio; CI, confidence interval; cART, combination Antiretroviral Therapy; EIP, EFA-identified inflammatory process

<sup>a</sup> Pre-cART era was defined as 1984 to June 30, 1996; and cART era was defined as July 1, 1996 to 2010.

<sup>b</sup> Adjusted variables were age, black race, college education, current smoking, obesity, HCV infection, alcohol intake and cocaine use since last visit; generalized gamma equations (GEE) utilized for analyses.

<sup>c</sup> Clinically relevant depressive symptoms defined as CES-D >20 compared to having not depressive symptoms defined as CES-D <12.

<sup>d</sup> Clinically relevant depressive symptoms defined as CES-D >20 or having antidepressant use compared to having not depressive symptoms defined as CES-D <12 and having no antidepressant use.



**Web Figure 1.** Adjusted logistic regressions of mild depressive symptoms (CES-D 12-20) and depressive symptoms (CES-D >20) on continuous estimates of EFA-identified inflammatory processes (EIPs) in HIV+ and HIV- person-visits in the MACS from 1984 to 2010. Adjusted multinomial logistic regression results showing that the association between continuous estimates of EFA-identified inflammatory process (EIP) 1 and 2 and mild depressive symptoms (CES-D 12-20) was significant among HIV+ persons. In contrast, such associations were not observed among HIV- persons. Abbreviations: MACS, the Multicenter AIDS Cohort Study; CES-D, Center for Epidemiology Study of Depression Scale; CI, confidence interval; EIP, EFA-identified inflammatory process