

## **Supplementary Information for**

Social stressors associated with age-related T lymphocyte percentages in older US adults: Evidence from the Health and Retirement Study.

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## Supplementary Information Text

### *Why T cells?*

T cells are particularly affected in age-related immune changes. As a result of thymic involution, fewer naïve T cells are produced, and as a result of exposure to immunological insults, more memory T cells accumulate. CCR7 expression is depressed as central memory T cells become less common and effector memory T cells more common. CD45RA re-expression in effector memory T cells has been linked to immunosenescence (1). As part of a normal infection cycle, T cells reduce expression of CD28 (a critical costimulatory marker) to avoid over-activation after the infection subsides. After repeated cycles of activation, an abundance of CD28<sup>-</sup> T cells (especially CD8<sup>+</sup>) accumulate. These cells are largely unable to respond to antigens, have limited reproductive ability, and generate inflammatory cytokines, potentially contributing to inflammaging (2). T lymphocytes may be of particular interest in light of the recent COVID-19 pandemic, given their important role in vaccine efficacy (2). Understanding variance in immunosenescence may be particularly important for understanding and combating age-related inequalities in vaccine efficacy and COVID-19 deaths.

### *Why these stressors?*

Past research on stress and health has emerged from a number of fields. This literature often uses similar term to refer to distinct phenomena and different terms to refer to similar concepts. We focus on social stressors—circumstances that arise from social position and experience that are expected to be stressful—that occur in adulthood. This concept is distinct from the psychological, cognitive, and affective responses to stressors often referred to as stress and from biological and physiological processes (e.g., oxidative stress and cellular damage (3)).

Past theory and research on stress and health has typically differentiated stressors by their timescale: acute negative events that resolve relatively quickly, daily events and hassles that are minor and happen frequently (4), chronic strains that represent ongoing difficulties (5), and life events that have a specific onset (6–8). Past research often also distinguishes life traumas as a subset of life events that represent major threats to a person's physical and mental wellbeing (6, 8). Research has demonstrated that these domains capture independent variance in health outcomes and immune functioning and are therefore all important to examine (7, 9).

The five stressors addressed in the current study—everyday discrimination, stressful life events, lifetime discrimination, life trauma, and chronic stress—represent daily hassles related to discrimination, life events from the prior five years, life events across the life course related to discrimination, life course exposure to major traumas, and ongoing chronic stressors, respectively. We thus address timescales of stress identified in the literature. Additionally, the discrimination-relevant measures (everyday discrimination and lifetime discrimination) may be particularly relevant to the population of older US adults in the current study experiencing ageism and age-related discrimination (10). Acute stress (i.e., immediate responses to circumstances that resolve over the course of minutes or hours) is typically studied in laboratory settings and is difficult to study in large population surveys (6). We therefore do not assess acute stress (using this definition of acute).

Consistent with many conceptualizations, we distinguish stressors by timescale (daily hassles, chronic, and life events). We also distinguish discrimination-related stressors from other stressors because past research suggests these stressors have distinct, independent effects on health (11). We also distinguish traumatic life events from other stressors, as is common in past research (6).

Though there is early evidence that social stress accelerates immune aging (4, 12–15), past research has focused on individual stressors, limiting the conclusions that can be drawn about

the effect of social stress on immune age phenotype, particularly with regard to the T cell compartment.

### *Supplemental Analyses*

Past research suggests that stressors are often interrelated and can affect one another. For instance, ongoing chronic stress may affect the way that daily stressors are perceived, coping strategies to deal with daily stressors, and health behaviors that may amplify the effects of daily stressors (6). We assess these stressors independently because 1) these stressors are well-established and each have extant literatures and 2) these scales are widely utilized, especially in studies of older adults, and are treated separately to aid in replication and comparison in samples from other settings (e.g., the English Longitudinal Study of Aging, the Mexican Health and Aging Study).

However, this literature suggests potential non-linear associations between stressors and immune aging. We assessed this possibility by regressing each immune aging variable on the interactions between each of the stressors. Only one of the fifty possible interactions was significantly significant. Participants who experienced greater chronic stress were less affected by everyday discrimination ( $b = -0.023$ ,  $se = 0.010$ ,  $p = 0.038$ ). This pattern of results suggests that there is not meaningful interactions among stressors.

Given that some of these stressor variables overlap in terms of timescale and/or stress domain, it is possible that they could be collapsed or combined to assess exposure to stressors more comprehensively. To assess whether these variables clustered together, we first assessed correlations among the stressor variables (see Table S7). Correlations were fairly modest, ranging from .10 to .37. We next estimated a principal components analysis (PCA) of these stressors (see Table S8). This analysis only produced one principal component (PC) with an eigenvalue greater than 1 which had relatively equal loadings for each stressor and explained only 37.67% of the variance. This suggests that there is only modest covariance among a subset of these variables.

Nevertheless, we regressed each immune aging variable on all but the final PC (see Figure S7). PC1 (relatively balanced on all five stressors) was significantly associated with all five immune aging measures. Only the association between this PC and late differentiated CD4<sup>+</sup> cell percentage remained significant after controlling for SES, lifestyle, and CMV seropositivity. PC2 (relatively high stressful life events and lifetime discrimination and relatively low chronic stress and everyday discrimination) was associated with a lower percentage of CD8<sup>+</sup> naïve cells in all models. Because the PCA did not support subdomains of stressors, this analysis is only suggestive and is not included in the main analysis. However, it appears that the general stress process may affect reactivation of latent viral infections and other processes that increase the percentage of late differentiated T cells; whereas, stressful life events may accelerate thymic involution, leading to a lower percentage of naïve T cells. More research is needed to confirm these associations and clarify their potential mechanisms.

Next, we also assessed structural equation models (SEMs) using the lavaan (16) and lavaan.survey (17) packages in R. We began by estimating a confirmatory factor analysis with a single factor representing cumulative stress exposure indicated by the five stressor variables. This model had poor model fit ( $\chi^2_{(df)} = 265.561_{(5)}$ ,  $p < .001$ ; CFI = .892; RMSEA = .095), suggesting that these variables do not load well onto a single underlying latent factor. Regardless, we estimated SEMs regressing all five outcomes on this latent factor simultaneously and then stepped in control variables (see Figure S8). This model was highly similar to results for PC1 above. This latent cumulative stress factor was significantly associated with all five immune aging measures. Only the association between this factor and late differentiated CD4<sup>+</sup> cell percentage remained significant after controlling for SES, lifestyle, and CMV seropositivity.

Finally, as a sensitivity analysis, we estimated SEMs regressing each stressor on all immune aging outcomes at once. Results are shown in Figure S9. Results were similar to those shown in the main analysis. The only differences statistical significance patterns were 1) terminally differentiated CD8+ cells were not significantly associated with stressful life events in any model and 2) late differentiated CD4+ cells were no longer associated with chronic stress in model 4. The parameter estimates were nearly identical across these models, suggesting that these differences in significance are due to power differences between these models.

#### *Why these mediators?*

Past research shows that the immune system is highly affected by the socioeconomic and lifestyle factors identified here (12, 18). These health lifestyle factors are all also strongly related to chronic and acute stress and life traumas (19). Similarly, people who experienced a greater number of major traumas or acute stressful events across the life course may have obtained less education. Thus, these socioeconomic and lifestyle factors may explain why exposure to these stressors is associated with immune age phenotypic T cell distributions.

CMV seropositivity is particularly important for immune aging (20, 21). Past research suggests that repeated reactivation of CMV over the life course depletes naïve T cell reserves—which additionally diminish with age due to thymic involution—and increase the number of late differential T cells. Recent research shows that CMV can be activated by social stress via activation of the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system (SNS) (22–24). Thus, controlling for CMV may explain why chronic stress is associated with more immune age phenotypic T cell distributions.

#### *Stress Measures*

Stressful life events was assessed using a 6-item count of stressful life events that occurred in the past five years, including “have you involuntarily lost a job for reasons other than retirement”, “have you been unemployed and looking for work for longer than 3 months”, “was anyone else in your household unemployed and looking for work for longer than 3 months”, “have you moved to a worse residence or neighborhood”, “were you robbed or did you have your home burglarized”, and “have you been the victim of fraud” (25). The most common stressful life event was having someone looking for a job in your household (endorsed by about 13% of respondents) and the least common was moving to a worse residence (endorsed by about 3% of respondents).

Chronic stress was assessed using an 8-item scale both the number ongoing stressful problems and how distressing these problems are, including “health problems (in yourself)”, “physical or emotional problems (in spouse or child)”, “alcohol or drug use in family member”, “difficulties at work”, “financial strain”, “housing problems”, “problems in a close relationship”, and “helping at least one sick, limited, or frail family member or friend on a regular basis” with responses ranging from 1 (*no, didn't happen*) to 4 (*yes, very upsetting*). Cronbach's  $\alpha$  for this scale is 0.64. Because chronic health problems could be confounded with immunosenescent leukocyte distribution, we also estimated the models using these same scales without that item. Results were highly similar with an identical pattern of significant results. We therefore use the full scale in all analyses. The most common chronic stressor was having an ongoing health problem (reported by about 67% of respondents) and the least common was ongoing housing problems (reported by about 17% of respondents).

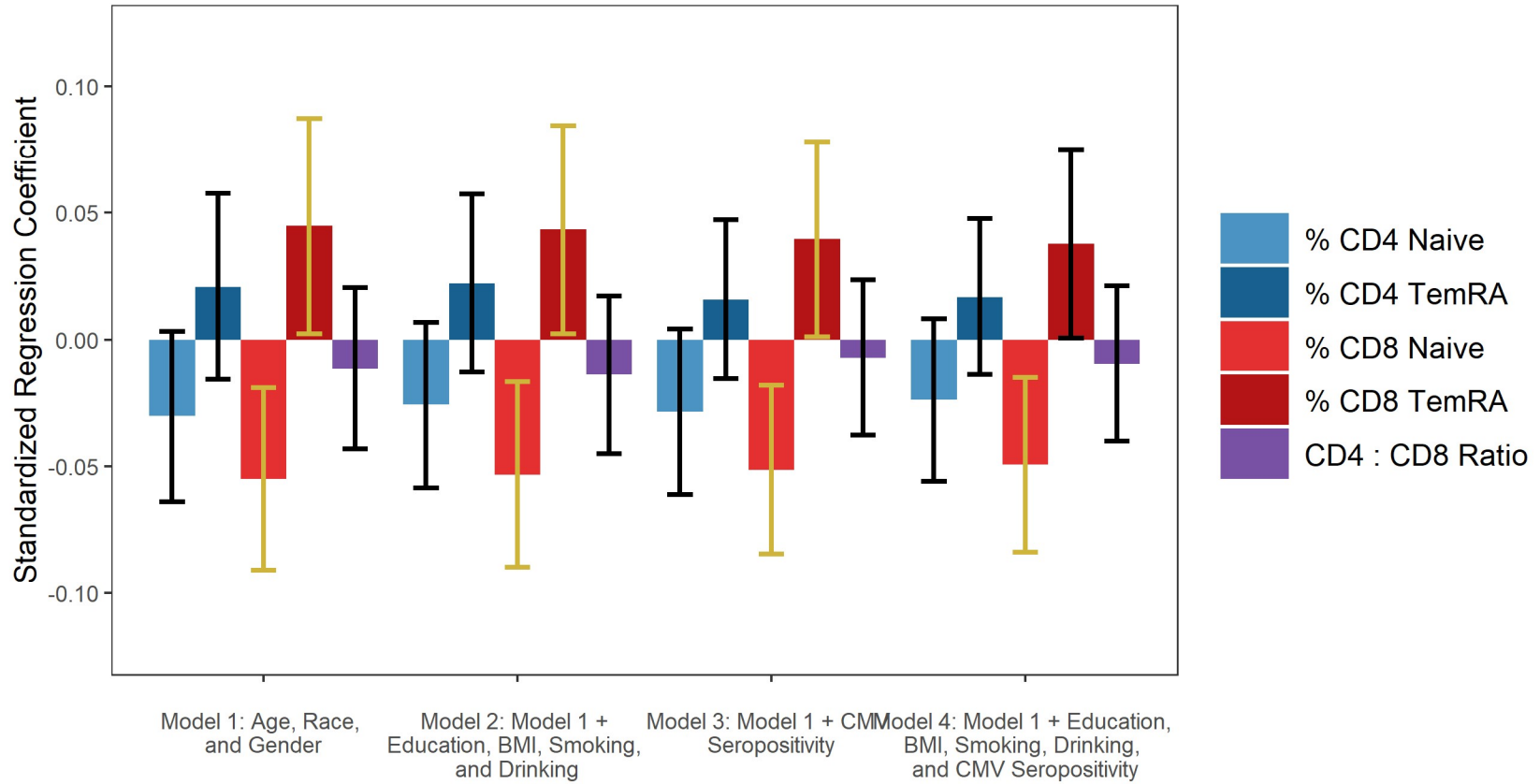
Everyday discrimination was assessed using a 6-item scale focused on everyday hassles and ongoing chronic stress related to perceived discrimination (26). Items included “you are treated with less courtesy or respect than other people”, “you receive poorer service than other people at restaurants or stores”, “people act as if they think you are not smart”, “people act as if they are afraid of you”, “you are threatened or harassed”, and “you receive poorer service or treatment than other people from doctors or hospitals”, with responses ranging from 1 (*never*) to 6 (*almost every day*). Cronbach's  $\alpha$  for this scale is 0.80. The level of discrimination reported by

respondents was highly similar to level reported in other studies (27). The most common form of discrimination reported was being treated with less courtesy or respect than other people (mean = 2.00) and the least common was receiving worse treatment from doctors or hospitals (mean = 1.23). Participants were also asked why they thought this happened to them. The most common first reason endorsed was age (endorsed by 1460 respondents), followed by gender (endorsed by 705 respondents), other reason (endorsed by 540 respondents), ancestry or national origin (endorsed by 424 respondents), race (endorsed by 319 respondents), weight (endorsed by 211 respondents), financial status (endorsed by 145 respondents), an aspect of their physical appearance (endorsed by 137 respondents), physical disability (endorsed by 92 respondents), religion (endorsed by 72 respondents), and sexual orientation (endorsed by 15 respondents).

Lifetime discrimination was assessed using a 7-item count of major stressful event related to discrimination throughout life, including "have you ever been unfairly dismissed from a job", "for unfair reasons, have you ever not been hired for a job", "have you ever been unfairly denied a promotion", "have you ever been unfairly prevented from moving into a neighborhood because the landlord or a realtor refused to sell or rent you a house or apartment", "have you ever been unfairly denied a bank loan", "have you ever been unfairly stopped, searched, questioned, physically threatened or abused by the police", and "have you ever been unfairly denied health care or treatment" (26). The most common form of discrimination was being dismissed from a job (endorsed by about 24% of respondents) and the least common was being prevented from moving to a neighborhood (endorsed by about 2% of respondents).

Life trauma was assessed using a count of 7 items focused on major traumatic events experienced throughout life, including "has a child of yours ever died", "have you ever been in a major fire, flood, earthquake, or other natural disaster", "have you ever fired a weapon in combat or been fired upon in combat", "has your spouse, partner, or child ever been addicted to drugs or alcohol", "were you the victim of a serious physical attack or assault in your life", "did you ever have a life-threatening illness or accident", and "did your spouse or a child of yours ever have a life-threatening illness or accident" (28). The most common trauma was having a spouse or child have a life-threatening illness (endorsed by about 25% of respondents) and the least common was firing a weapon or being fired upon in combat (endorsed by about 5% of respondents).

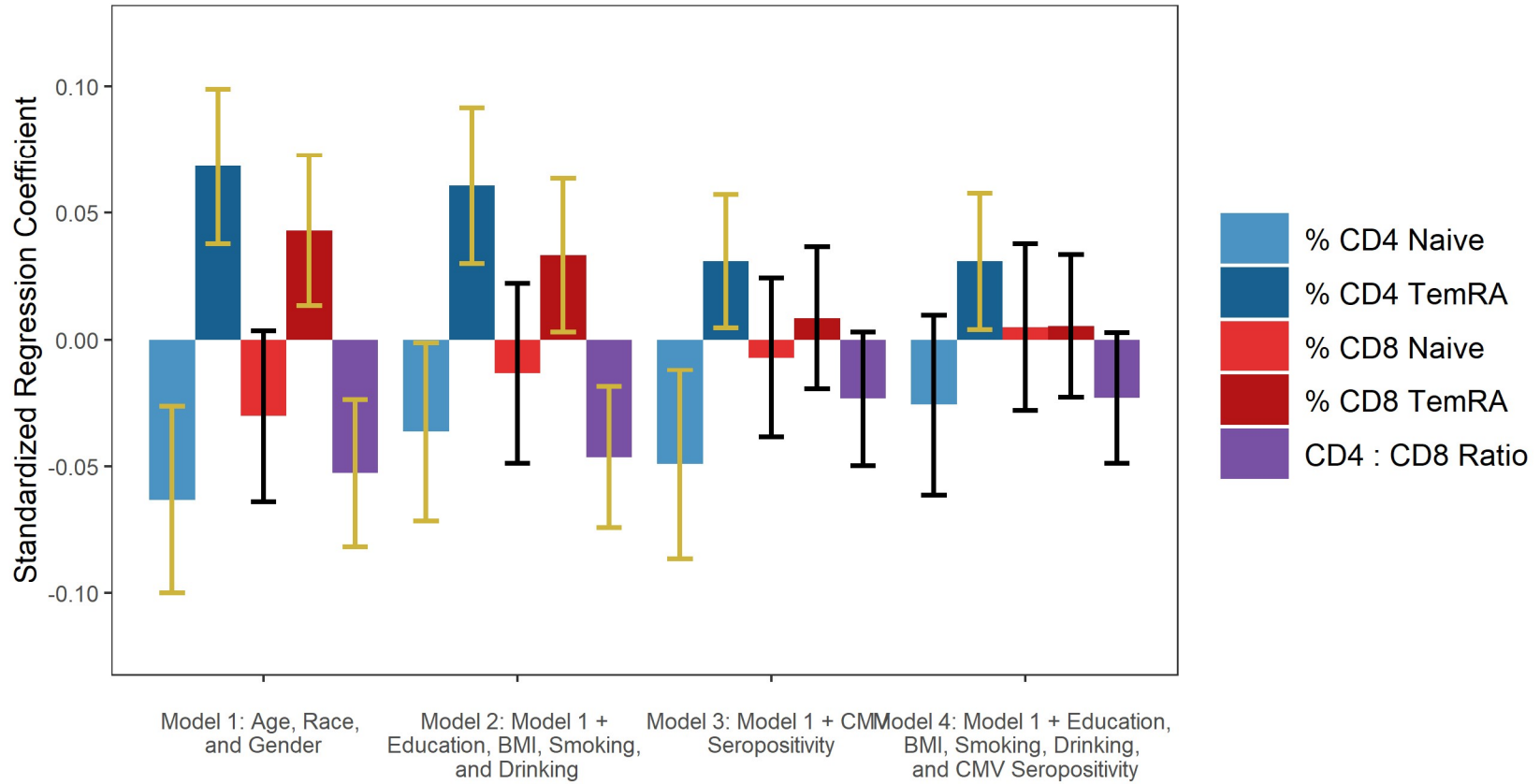
## Stressful Life Events



**Fig. S1.** Results for Stressful Life Events

Note: TemRA = terminally differentiated; gold confidence intervals indicate a statistically significant difference from 0.

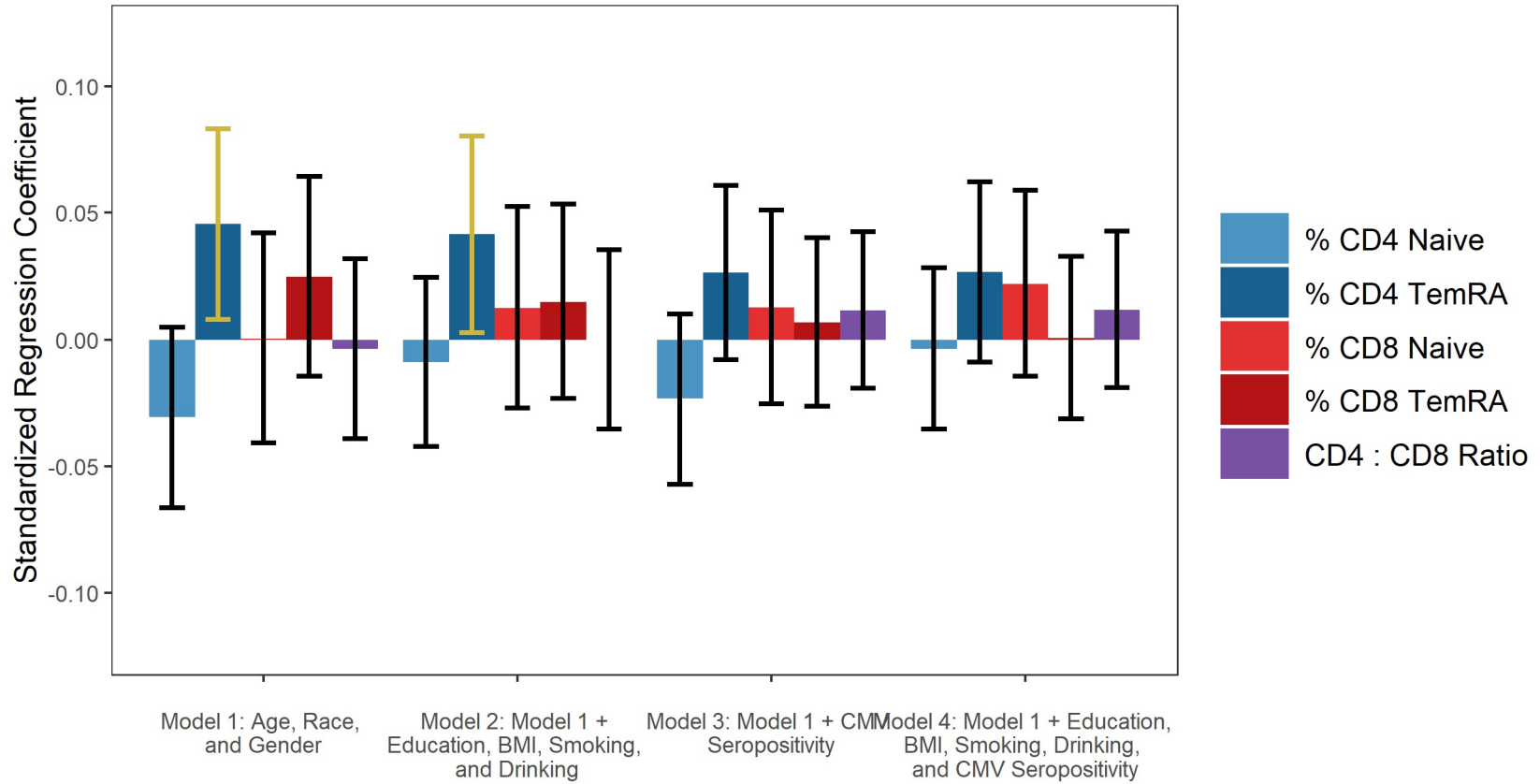
## Chronic Stress



**Fig. S2.** Results for Chronic Stress

Note: TemRA = terminally differentiated; gold confidence intervals indicate a statistically significant difference from 0.

## Everyday Discrimination

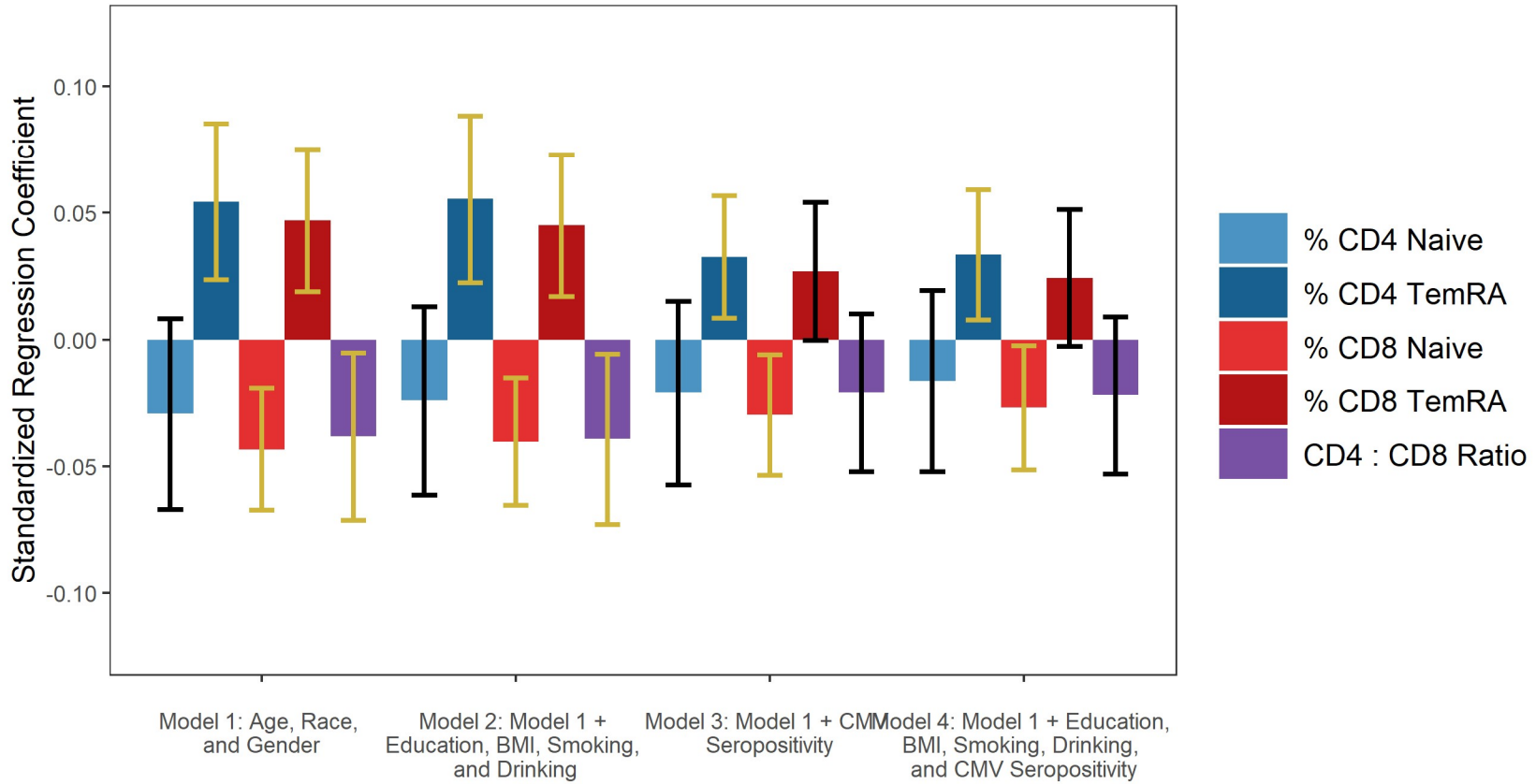


**Fig. S3.** Results for Everyday Discrimination

Note: TemRA = terminally differentiated; gold confidence intervals indicate a statistically significant difference from 0.

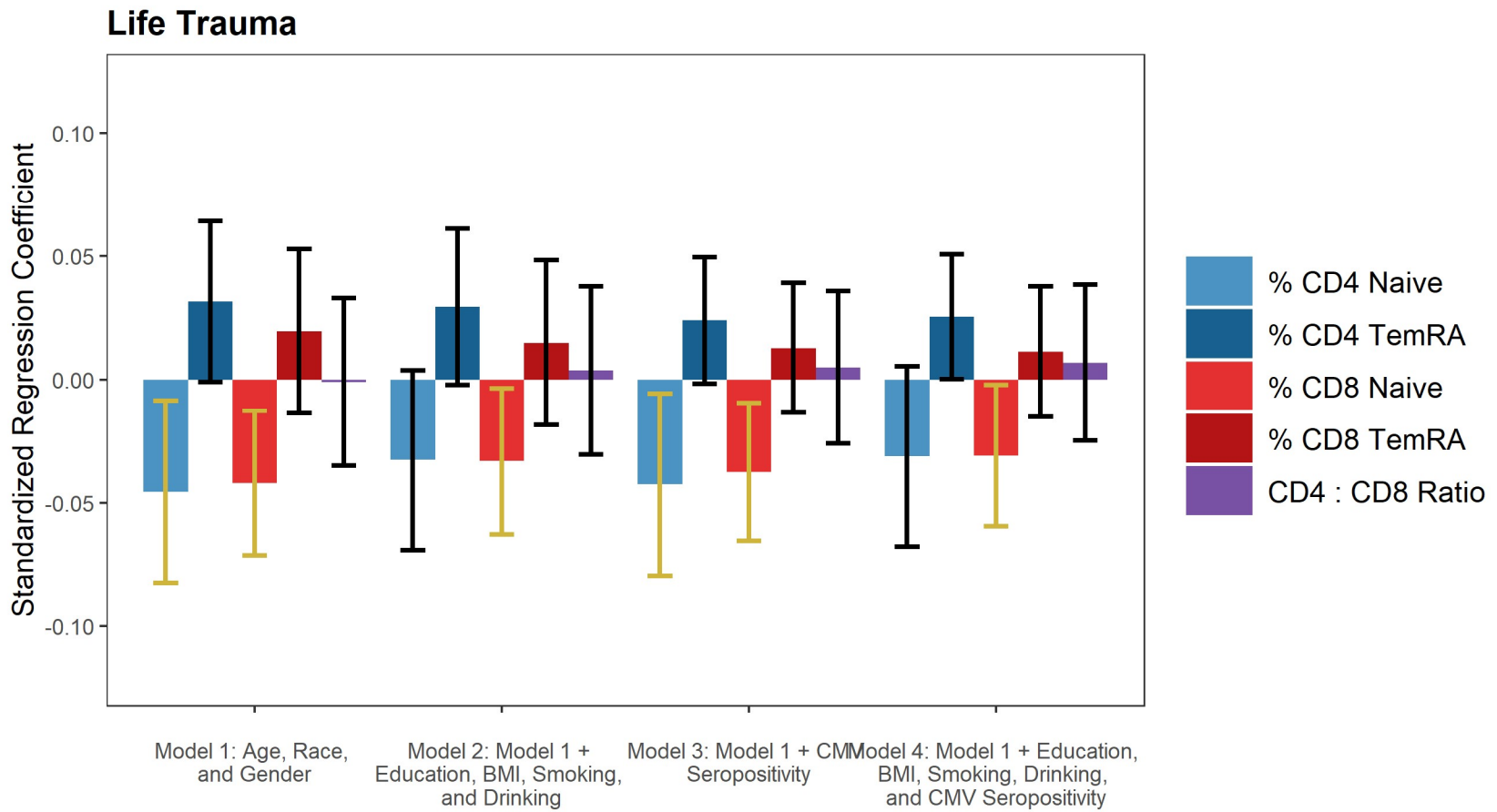


## Lifetime Discrimination



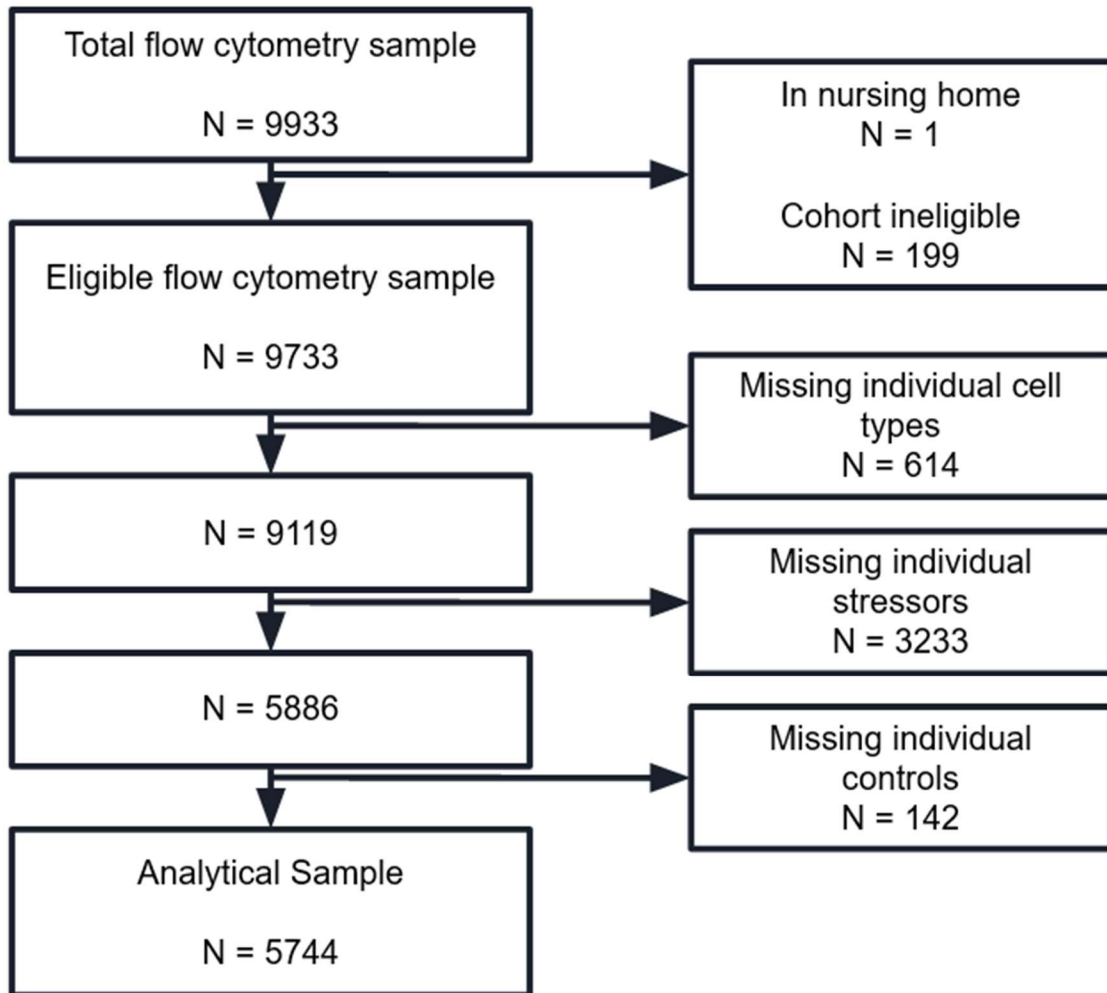
**Fig. S4.** Results for Lifetime Discrimination

Note: TemRA = terminally differentiated; gold confidence intervals indicate a statistically significant difference from 0.

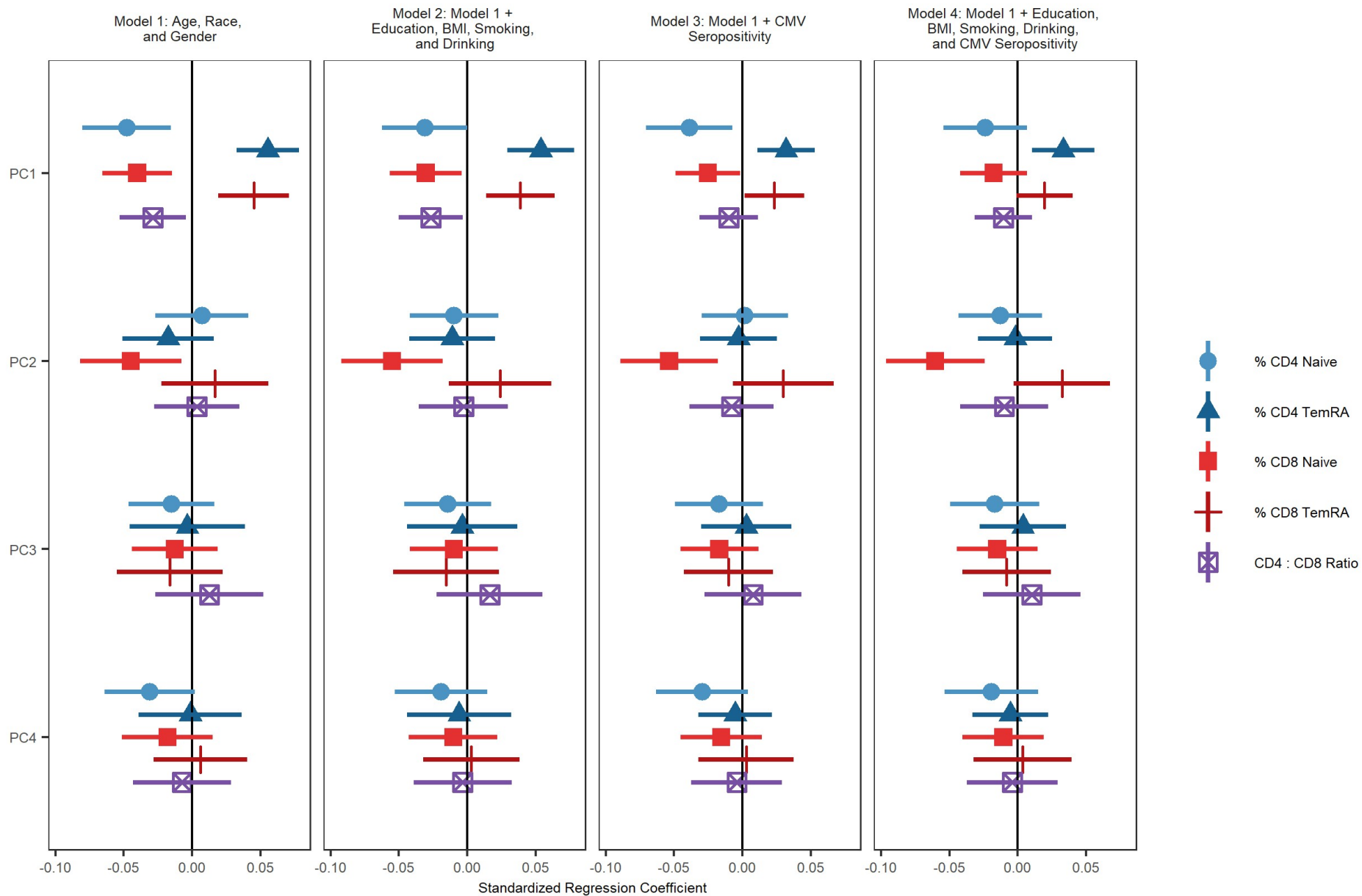


**Fig. S5.** Results for Life Trauma

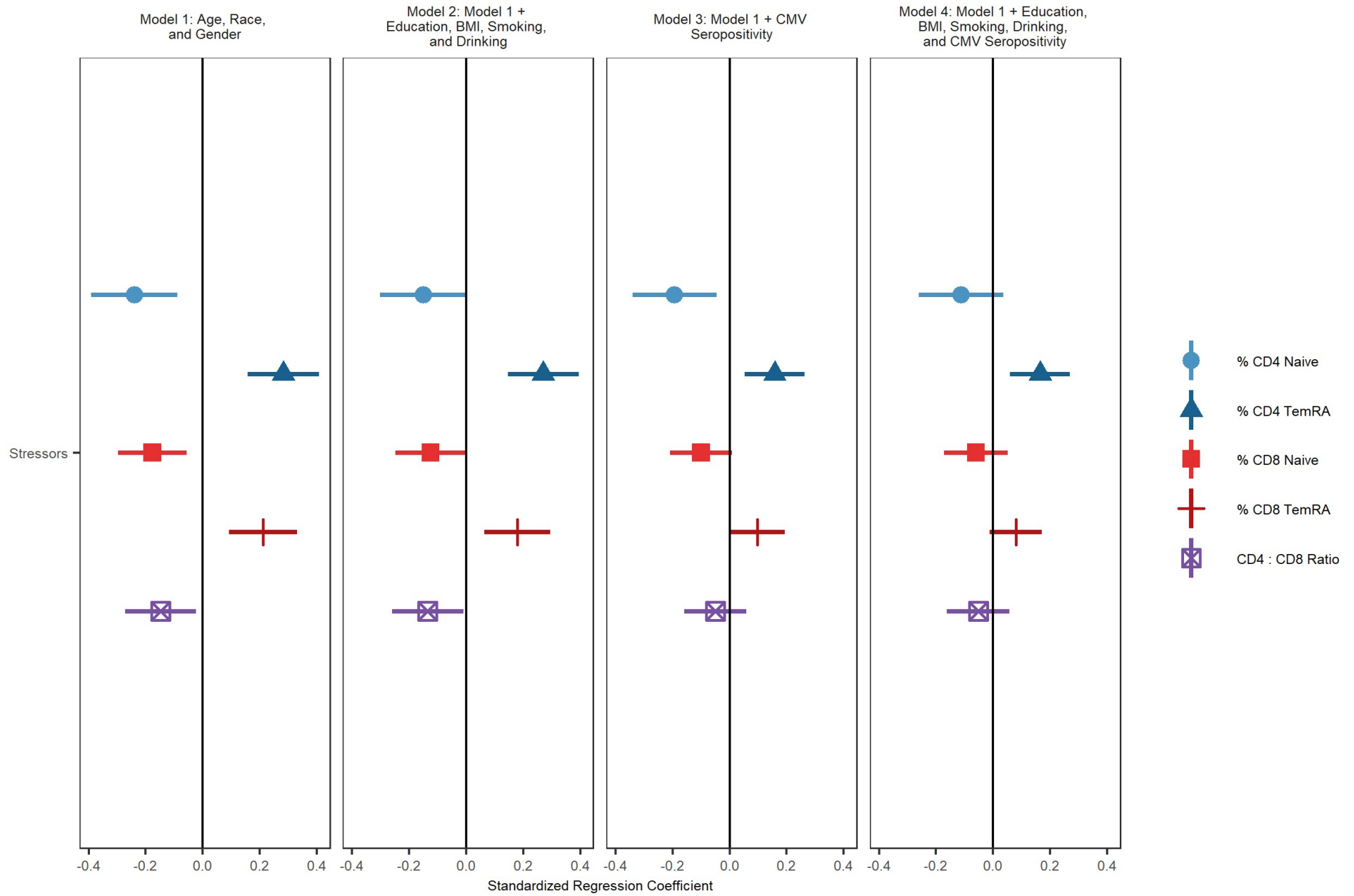
Note: TemRA = terminally differentiated; gold confidence intervals indicate a statistically significant difference from 0.



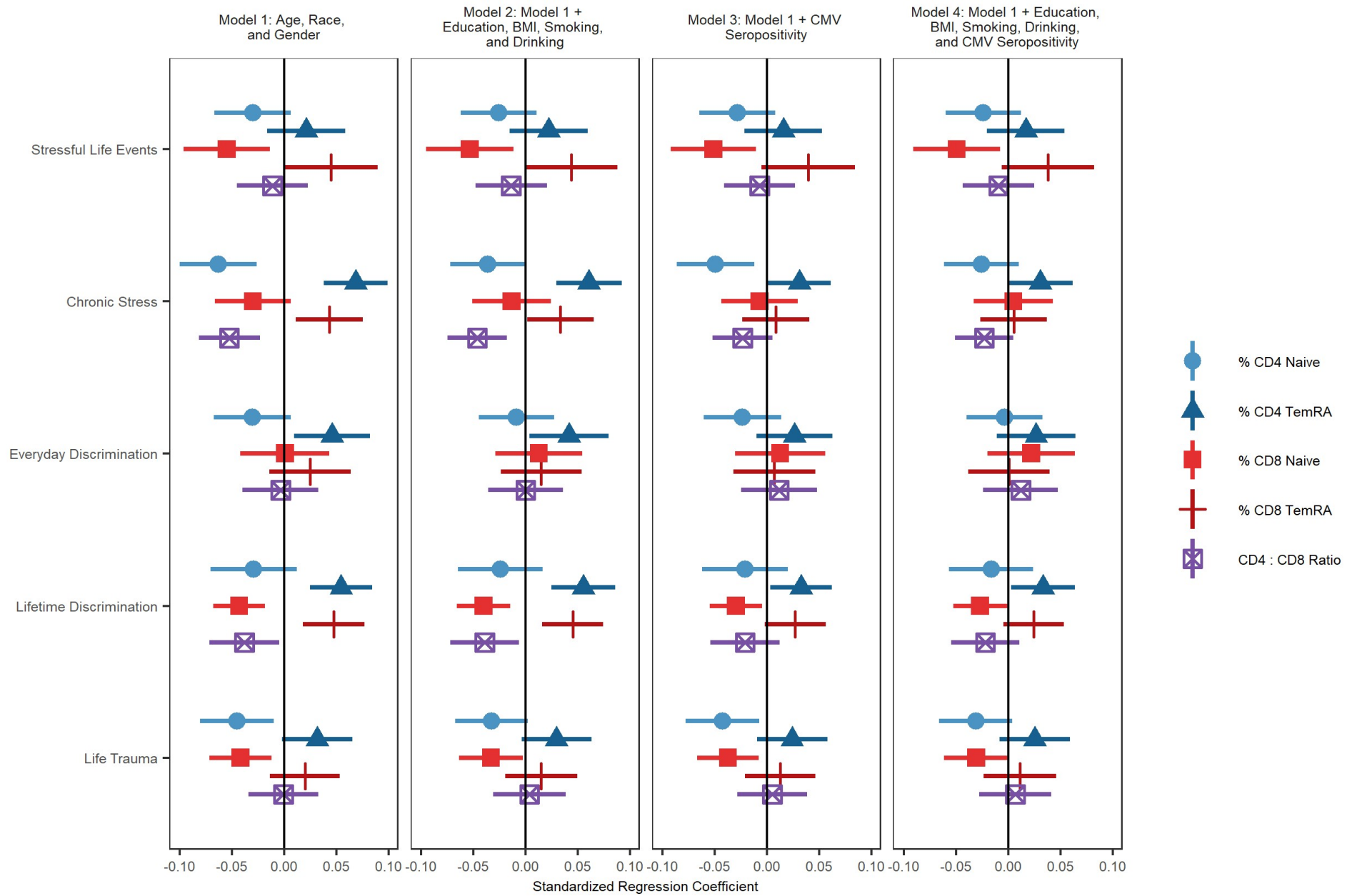
**Fig. S6.** Sample Diagram



**Fig. S7.** Regression coefficients and 95% confidence intervals from nested analyses regressing cell subset percentage/ratio on stressor PCAs. All models control for age, race, and gender. TemRA = terminally differentiated.



**Fig. S8.** SEM coefficients and 95% confidence intervals from nested analyses regressing cell subset percentage/ratio on CFA of stressors. All models control for age, race, and gender. TemRA = terminally differentiated.



**Fig. S9.** SEM coefficients and 95% confidence intervals from nested analyses regressing all cell subset percentage/ratios simultaneously on each stressor. All models control for age, race, and gender. TemRA = terminally differentiated.

**Table S1.** Descriptive statistics.

	Mean/ Proportion	SD	Range		
CD4 <sup>+</sup> TemRA	-4.39	1.50	-9.21	-	-0.34
CD4 <sup>+</sup> Naïve	0.46	0.18	0	-	0.95
CD8 <sup>+</sup> TemRA	0.43	0.22	0	-	0.97
CD8 <sup>+</sup> Naïve	0.24	0.16	0	-	0.90
CD4 <sup>+</sup> :CD8 <sup>+</sup> Ratio	1.15	0.71	-2.37	-	3.68
Stressful Life Events	0.50	0.84	0	-	6
Chronic Stress	12.56	3.77	8	-	32
Everyday Discrimination	1.54	0.65	1	-	6
Lifetime Discrimination	0.65	1.00	0	-	7
Life Trauma	1.09	1.12	0	-	6
Age	68.34	9.23	50	-	107
Gender (Female = 1)	0.55				
Race					
White, not Hispanic	0.85				
Black, not Hispanic	0.07				
Hispanic	0.06				
Other, not Hispanic	0.02				
Education					
16+ Years	0.33				
0-11 Years	0.10				
12 Years	0.31				
13-15 Years	0.26				
BMI					
Under/Normal Weight	0.27				
Overweight	0.37				
Obese 1	0.22				
Obese 2	0.14				
Smoking					
Never Smoked	0.45				
Current Smoker	0.09				
Past Smoker	0.45				
Alcohol Use					
Non-Drinker	0.54				
1-4 Drinks per day	0.45				
5+ Drinks per day	0.02				
CMV Seropositivity					
Non-Reactive	0.39				
Borderline	0.02				
Reactive	0.59				

Note: SD = standard deviation, TemRA = terminally differentiated; proportions may not sum to 1 due to rounding; T cell percentages / ratios and stressors are not standardized in this table; CD4<sup>+</sup> TemRA and the CD4<sup>+</sup>:CD8<sup>+</sup> ratio are log transformed to approximate a normal distribution (see method section).

**Table S2.** Full results for late differentiated CD4+ percentage.

	I		II		III		IV		V		VI		VII		VIII		IX		X		XI		XII		XIII		XIV		XV		XVI		XVII		XVIII		XIX		XX			
	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p				
Everyday Discrimination	0.046	0.022	0.042	0.042	0.026	0.138	0.027	0.148																																		
Stressful Life Events							0.021	0.271	0.022	0.223	0.016	0.332	0.017	0.291																												
Lifetime Discrimination													0.054	0.001	0.055	0.002	0.032	0.011	0.033	0.015																						
Life Trauma																						0.031	0.064	0.029	0.075	0.024	0.072	0.025	0.056													
Chronic Stress																																		0.068	0.000	0.061	0.000	0.031	0.026	0.031	0.030	
Age	0.016	0.000	0.014	0.000	0.005	0.002	0.005	0.004	0.016	0.000	0.014	0.000	0.005	0.000	0.005	0.002	0.016	0.000	0.014	0.000	0.005	0.001	0.005	0.003	0.015	0.000	0.013	0.000	0.004	0.004	0.004	0.009	0.016	0.000	0.014	0.000	0.005	0.001	0.005	0.003		
Gender (Female = 1)	0.123	0.001	0.088	0.021	0.016	0.574	0.003	0.929	0.118	0.001	0.083	0.027	0.014	0.635	0.000	0.994	0.130	0.001	0.095	0.013	0.021	0.482	0.007	0.825	0.116	0.002	0.081	0.033	0.012	0.679	-0.002	0.955	0.106	0.005	0.073	0.059	0.008	0.788	-0.006	0.851		
Race																																										
Black, not Hispanic	0.421	0.000	0.376	0.000	0.091	0.031	0.089	0.041	0.430	0.000	0.380	0.000	0.095	0.027	0.091	0.039	0.405	0.000	0.355	0.000	0.081	0.052	0.077	0.074	0.428	0.000	0.379	0.000	0.094	0.024	0.090	0.036	0.419	0.000	0.377	0.000	0.092	0.030	0.091	0.037		
Hispanic	0.390	0.000	0.335	0.000	0.006	0.914	0.013	0.819	0.381	0.000	0.325	0.000	0.000	0.996	0.005	0.927	0.381	0.000	0.321	0.000	0.001	0.985	0.004	0.940	0.381	0.000	0.325	0.000	0.000	0.998	0.005	0.924	0.382	0.000	0.331	0.000	0.002	0.965	0.010	0.862		
Other, not Hispanic	0.130	0.160	0.108	0.248	-0.176	0.054	-0.186	0.042	0.134	0.144	0.110	0.237	-0.175	0.054	-0.186	0.042	0.132	0.149	0.107	0.245	-0.175	0.053	-0.186	0.040	0.135	0.146	0.111	0.236	-0.175	0.054	-0.186	0.041	0.132	0.145	0.109	0.230	-0.174	0.053	-0.184	0.041		
Education																																										
0-11 Years			0.137	0.011			-0.038	0.406			0.144	0.009			-0.034	0.470			0.154	0.006			-0.027	0.565			0.143	0.009			-0.034	0.463			0.131	0.016			-0.041	0.384		
12 Years			0.084	0.044			-0.009	0.803			0.085	0.040			-0.008	0.816			0.090	0.031			-0.005	0.887			0.084	0.041			-0.009	0.804			0.082	0.046			-0.010	0.777		
13-15 Years			-0.018	0.688			-0.078	0.049			-0.019	0.665			-0.079	0.044			-0.020	0.650			-0.080	0.047			-0.021	0.638			-0.081	0.042			-0.022	0.609			-0.080	0.043		
BMI																																										
Overweight			-0.009	0.825			-0.011	0.755			-0.009	0.821			-0.011	0.749			-0.010	0.801			-0.012	0.741			-0.007	0.868			-0.010	0.788			-0.010	0.808			-0.011	0.748		
Obese 1			-0.035	0.425			-0.030	0.428			-0.034	0.431			-0.030	0.429			-0.037	0.385			-0.032	0.408			-0.033	0.449			-0.029	0.443			-0.038	0.385			-0.031	0.411		
Obese 2			-0.039	0.430			-0.024	0.652			-0.030	0.561			-0.019	0.728			-0.037	0.476			-0.022	0.682			-0.029	0.561			-0.019	0.727			-0.047	0.348			-0.026	0.624		
Smoking																																										
Current Smoker			0.190	0.000			0.097	0.041			0.193	0.000			0.099	0.045			0.180	0.001			0.092	0.055			0.188	0.000			0.094	0.043			0.175	0.001			0.090	0.060		
Past Smoker			-0.038	0.348			-0.032	0.328			-0.035	0.381			-0.030	0.355			-0.042	0.293			-0.035	0.291			-0.040	0.316			-0.035	0.293			-0.044	0.275			-0.035	0.290		
Alcohol Use																																										
1-4 Drinks per day			-0.098	0.016			-0.049	0.204			-0.103	0.010			-0.052	0.170			-0.100	0.013			-0.050	0.186			-0.099	0.012			-0.049	0.196			-0.094	0.017			-0.048	0.206		
5+ Drinks per day			-0.467	0.000			-0.246	0.020			-0.464	0.000			-0.244	0.022			-0.451	0.000			-0.236	0.025			-0.465	0.000			-0.245	0.021			-0.457	0.000			-0.241	0.021		
CMV Seropositivity																																										
Borderline					0.532	0.000	0.537	0.000			0.534	0.000	0.539	0.000					0.531	0.000	0.536	0.000					0.530	0.000	0.536	0.000												
Reactive					1.036	0.000	1.027	0.000			1.038	0.000	1.029	0.000					1.035	0.000	1.026	0.000					1.038	0.000	1.029	0.000												
Intercept	-1.321	0.000	-1.137	0.000	-1.077	0.000	-0.972	0.000	-1.298	0.000	-1.122	0.000	-1.071	0.000	-0.967	0.000	-1.322	0.000	-1.134	0.000	-1.079	0.000	-0.969	0.000	-1.231	0.000	-1.055	0.000	-1.020	0.000	-0.913	0.000	-1.326	0.000	-1.133	0.000	-1.072	0.000	-0.964	0.000		



**Table S3.** Full results for naïve CD4<sup>+</sup> percentage.

	I		II		III		IV		V		VI		VII		VIII		IX		X		XI		XII		XIII		XIV		XV		XVI		XVII		XVIII		XIX		XX			
	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p				
Everyday Discrimination	-0.031	0.096	-0.009	0.604	-0.023	0.178	-0.004	0.827																																		
Stressful Life Events Lifetime Discrimination									-0.030	0.083	-0.026	0.129	-0.028	0.094	-0.024	0.151																										
Life Trauma																																										
Chronic Stress																																										
Age	-0.008	0.000	-0.008	0.000	-0.004	0.016	-0.004	0.009	-0.009	0.000	-0.008	0.000	-0.005	0.010	-0.005	0.004	-0.008	0.000	-0.008	0.000	-0.004	0.020	-0.005	0.007	-0.007	0.000	-0.007	0.000	-0.003	0.080	-0.004	0.027	-0.009	0.000	-0.008	0.000	-0.005	0.006	-0.005	0.004		
Gender (Female = 1)	0.274	0.000	0.298	0.000	0.314	0.000	0.328	0.000	0.276	0.000	0.297	0.000	0.315	0.000	0.327	0.000	0.271	0.000	0.294	0.000	0.313	0.000	0.325	0.000	0.279	0.000	0.299	0.000	0.318	0.000	0.329	0.000	0.288	0.000	0.304	0.000	0.325	0.000	0.332	0.000		
Race																																										
Black, not Hispanic	-0.664	0.000	-0.557	0.000	-0.539	0.000	-0.456	0.000	-0.668	0.000	-0.555	0.000	-0.541	0.000	-0.453	0.000	-0.657	0.000	-0.547	0.000	-0.534	0.000	-0.448	0.000	-0.665	0.000	-0.555	0.000	-0.538	0.000	-0.453	0.000	-0.659	0.000	-0.556	0.000	-0.537	0.000	-0.455	0.000		
Hispanic	-0.377	0.000	-0.271	0.000	-0.232	0.000	-0.156	0.021	-0.371	0.000	-0.267	0.000	-0.226	0.000	-0.154	0.021	-0.371	0.000	-0.267	0.000	-0.227	0.000	-0.154	0.021	-0.370	0.000	-0.268	0.000	-0.226	0.001	-0.154	0.022	-0.372	0.000	-0.272	0.000	-0.230	0.000	-0.158	0.018		
Other, not Hispanic	-0.087	0.289	-0.056	0.473	0.029	0.704	0.048	0.524	-0.087	0.286	-0.052	0.501	0.031	0.685	0.053	0.480	-0.089	0.270	-0.055	0.479	0.027	0.718	0.049	0.506	-0.087	0.291	-0.054	0.497	0.030	0.693	0.051	0.496	-0.086	0.286	-0.055	0.481	0.028	0.711	0.049	0.514		
Education																																										
0-11 Years			-0.250	0.000			-0.187	0.002			-0.253	0.000			-0.190	0.002			-0.256	0.000			-0.192	0.002			-0.252	0.000			-0.190	0.002			-0.244	0.000			-0.184	0.003		
12 Years			-0.147	0.000			-0.114	0.001			-0.149	0.000			-0.116	0.001			-0.150	0.000			-0.116	0.001			-0.148	0.000			-0.115	0.001			-0.146	0.000			-0.114	0.001		
13-15 Years			-0.066	0.110			-0.045	0.268			-0.064	0.122			-0.043	0.290			-0.065	0.118			-0.044	0.278			-0.063	0.133			-0.041	0.309			-0.063	0.128			-0.043	0.291		
BMI																																										
Overweight			-0.082	0.052			-0.081	0.046			-0.080	0.058			-0.079	0.052			-0.081	0.054			-0.080	0.047			-0.083	0.046			-0.082	0.040			-0.081	0.055			-0.080	0.048		
Obese 1			-0.175	0.001			-0.176	0.001			-0.173	0.001			-0.174	0.001			-0.173	0.001			-0.175	0.001			-0.174	0.001			-0.175	0.001			-0.172	0.001			-0.174	0.001		
Obese 2			-0.323	0.000			-0.328	0.000			-0.321	0.000			-0.325	0.000			-0.321	0.000			-0.326	0.000			-0.322	0.000			-0.326	0.000			-0.326	0.000			-0.321	0.000		
Smoking																																										
Current Smoker			-0.155	0.011			-0.122	0.053			-0.152	0.011			-0.119	0.056			-0.149	0.011			-0.118	0.055			-0.147	0.014			-0.114	0.068			-0.143	0.016			-0.114	0.066		
Past Smoker			0.020	0.582			0.018	0.593			0.019	0.594			0.017	0.599			0.022	0.534			0.020	0.554			0.025	0.491			0.023	0.494			0.024	0.495			0.021	0.522		
Alcohol Use																																										
1-4 Drinks per day			0.125	0.004			0.107	0.014			0.126	0.004			0.108	0.013			0.124	0.004			0.107	0.014			0.121	0.005			0.104	0.017			0.121	0.005			0.104	0.017		
5+ Drinks per day			-0.001	0.991			-0.080	0.559			-0.003	0.983			-0.081	0.557			-0.008	0.950			-0.084	0.542			-0.001	0.991			-0.080	0.565			-0.007	0.959			-0.083	0.545		
CMV Seropositivity																																										
Borderline					-0.219	0.173	-0.189	0.237					-0.223	0.167	-0.192	0.229					-0.218	0.178	-0.188	0.240					-0.216	0.186	-0.187	0.245					-0.212	0.180	-0.186	0.241		
Reactive					-0.393	0.000	-0.365	0.000					-0.394	0.000	-0.365	0.000					-0.393	0.000	-0.364	0.000					-0.393	0.000	-0.365	0.000					-0.387	0.000	-0.362	0.000		
Intercept	0.577	0.000	0.662	0.000	0.485	0.000	0.603	0.000	0.593	0.000	0.693	0.000	0.508	0.000	0.639	0.000	0.569	0.000	0.672	0.000	0.477	0.000	0.613	0.000	0.495	0.001	0.617	0.000	0.416	0.003	0.567	0.000	0.598	0.000	0.680	0.000	0.503	0.000	0.620	0.000		

**Table S4.** Full results for late differentiated CD8+ percentage.

	I		II		III		IV		V		VI		VII		VIII		IX		X		XI		XII		XIII		XIV		XV		XVI		XVII		XVIII		XIX		XX		
	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p			
Everyday Discrimination	0.025	0.226	0.015	0.452	0.007	0.688	0.001	0.968																																	
Stressful Life Events Lifetime Discrimination									0.045	0.044	0.043	0.045	0.040	0.050	0.038	0.054																									
Life Trauma																										0.020	0.255	0.015	0.387	0.013	0.344	0.011	0.411								
Chronic Stress																																									
Age	0.036	0.000	0.035	0.000	0.026	0.000	0.026	0.000	0.037	0.000	0.036	0.000	0.027	0.000	0.027	0.000	0.036	0.000	0.035	0.000	0.026	0.000	0.026	0.000	0.035	0.000	0.034	0.000	0.025	0.000	0.026	0.000	0.036	0.000	0.035	0.000	0.026	0.000	0.026	0.000	
Gender (Female = 1)	-0.060	0.076	-0.082	0.015	-0.158	0.000	-0.161	0.000	-0.060	0.071	-0.080	0.015	-0.156	0.000	-0.158	0.000	-0.052	0.126	-0.073	0.032	-0.152	0.000	-0.155	0.000	-0.064	0.060	-0.084	0.013	-0.159	0.000	-0.161	0.000	-0.070	0.040	-0.088	0.009	-0.161	0.000	-0.162	0.000	
Race																																									
Black, not Hispanic	0.116	0.049	0.070	0.236	-0.188	0.000	-0.199	0.000	0.115	0.052	0.067	0.263	-0.192	0.000	-0.204	0.000	0.098	0.105	0.050	0.412	-0.199	0.000	-0.211	0.000	0.119	0.042	0.071	0.228	-0.188	0.000	-0.200	0.000	0.113	0.053	0.070	0.239	-0.188	0.000	-0.200	0.000	
Hispanic	0.288	0.000	0.249	0.000	-0.066	0.139	-0.055	0.153	0.282	0.000	0.243	0.000	-0.068	0.132	-0.057	0.147	0.283	0.000	0.242	0.000	-0.067	0.141	-0.056	0.155	0.283	0.000	0.246	0.000	-0.067	0.138	-0.055	0.161	0.284	0.000	0.249	0.000	-0.067	0.140	-0.054	0.168	
Other, not Hispanic	0.214	0.026	0.182	0.045	-0.069	0.380	-0.095	0.212	0.209	0.027	0.175	0.054	-0.076	0.341	-0.103	0.184	0.213	0.025	0.178	0.048	-0.071	0.371	-0.098	0.202	0.215	0.021	0.182	0.041	-0.070	0.369	-0.097	0.202	0.214	0.025	0.181	0.045	-0.069	0.380	-0.095	0.210	
Education																																									
0-11 Years			0.072	0.208			-0.091	0.097			0.078	0.169			-0.087	0.110			0.084	0.144			-0.085	0.123			0.075	0.191			-0.090	0.099			0.068	0.237			-0.091	0.096	
12 Years			0.048	0.297			-0.038	0.362			0.050	0.266			-0.035	0.390			0.053	0.254			-0.035	0.406			0.048	0.294			-0.038	0.365			0.046	0.310			-0.038	0.360	
13-15 Years			0.041	0.363			-0.015	0.703			0.037	0.401			-0.018	0.646			0.038	0.390			-0.016	0.680			0.039	0.380			-0.016	0.678			0.038	0.390			-0.015	0.692	
BMI																																									
Overweight			0.057	0.111			0.055	0.099			0.054	0.129			0.053	0.117			0.055	0.117			0.054	0.105			0.058	0.107			0.055	0.096			0.056	0.118			0.055	0.099	
Obese 1			0.092	0.042			0.098	0.011			0.089	0.047			0.094	0.014			0.089	0.046			0.096	0.013			0.093	0.040			0.098	0.012			0.090	0.046			0.098	0.012	
Obese 2			0.192	0.001			0.207	0.000			0.188	0.001			0.199	0.000			0.188	0.001			0.202	0.000			0.195	0.000			0.206	0.000			0.185	0.001			0.205	0.000	
Smoking																																									
Current Smoker			-0.096	0.064			-0.184	0.000			-0.101	0.053			-0.189	0.000			-0.107	0.043			-0.190	0.000			-0.098	0.060			-0.187	0.000			-0.106	0.045			-0.185	0.000	
Past Smoker			-0.010	0.741			-0.004	0.854			-0.009	0.773			-0.004	0.866			-0.015	0.615			-0.008	0.747			-0.012	0.707			-0.006	0.799			-0.014	0.638			-0.005	0.826	
Alcohol Use																																									
1-4 Drinks per day			-0.094	0.004			-0.046	0.104			-0.097	0.003			-0.048	0.095			-0.093	0.004			-0.045	0.113			-0.094	0.004			-0.045	0.121			-0.091	0.005			-0.046	0.117	
5+ Drinks per day			-0.195	0.028			0.013	0.885			-0.193	0.036			0.014	0.880			-0.183	0.042			0.018	0.836			-0.194	0.029			0.012	0.887			-0.190	0.035			0.013	0.879	
CMV Seropositivity																																									
Borderline					0.304	0.016	0.308	0.016					0.310	0.015	0.314	0.014					0.304	0.018	0.308	0.017					0.304	0.017	0.308	0.016					0.303	0.017	0.308	0.016	
Reactive					0.953	0.000	0.964	0.000					0.953	0.000	0.964	0.000					0.951	0.000	0.962	0.000					0.953	0.000	0.964	0.000					0.952	0.000	0.964	0.000	
Intercept	-2.549	0.000	-2.512	0.000	-2.319	0.000	-2.354	0.000	-2.603	0.000	-2.566	0.000	-2.387	0.000	-2.416	0.000	-2.571	0.000	-2.534	0.000	-2.342	0.000	-2.375	0.000	-2.498	0.000	-2.478	0.000	-2.298	0.000	-2.341	0.000	-2.558	0.000	-2.520	0.000	-2.318	0.000	-2.357	0.000	

**Table S5.** Full results for naïve CD8<sup>+</sup> percentage.

	I		II		III		IV		V		VI		VII		VIII		IX		X		XI		XII		XIII		XIV		XV		XVI		XVII		XVIII		XIX		XX		
	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p			
Everyday Discrimination	0.001	0.981	0.013	0.540	0.013	0.521	0.022	0.248																																	
Stressful Life Events Lifetime Discrimination									-0.055	0.004	-0.053	0.007	-0.051	0.004	-0.049	0.007																									
Life Trauma Chronic Stress																																									
Age	-0.042	0.000	-0.041	0.000	-0.035	0.000	-0.035	0.000	-0.043	0.000	-0.043	0.000	-0.037	0.000	-0.037	0.000	-0.043	0.000	-0.042	0.000	-0.036	0.000	-0.036	0.000	-0.041	0.000	-0.041	0.000	-0.035	0.000	-0.035	0.000	-0.042	0.000	-0.041	0.000	-0.035	0.000	-0.035	0.000	
Gender (Female = 1)	0.363	0.000	0.380	0.000	0.430	0.000	0.432	0.000	0.358	0.000	0.373	0.000	0.422	0.000	0.424	0.000	0.352	0.000	0.368	0.000	0.420	0.000	0.422	0.000	0.363	0.000	0.378	0.000	0.427	0.000	0.428	0.000	0.368	0.000	0.380	0.000	0.428	0.000	0.428	0.000	
Race																																									
Black, not Hispanic	0.294	0.000	0.356	0.000	0.499	0.000	0.533	0.000	0.302	0.000	0.366	0.000	0.509	0.000	0.543	0.000	0.316	0.000	0.379	0.000	0.517	0.000	0.549	0.000	0.301	0.000	0.362	0.000	0.508	0.000	0.540	0.000	0.300	0.000	0.360	0.000	0.503	0.000	0.536	0.000	
Hispanic	-0.279	0.000	-0.211	0.003	-0.039	0.511	-0.011	0.851	-0.278	0.000	-0.210	0.003	-0.041	0.506	-0.013	0.821	-0.278	0.000	-0.210	0.003	-0.042	0.491	-0.015	0.804	-0.278	0.000	-0.213	0.003	-0.041	0.503	-0.015	0.796	-0.279	0.000	-0.215	0.003	-0.042	0.486	-0.016	0.790	
Other, not Hispanic	-0.111	0.317	-0.100	0.369	0.081	0.441	0.082	0.432	-0.101	0.358	-0.087	0.431	0.092	0.374	0.095	0.360	-0.107	0.339	-0.093	0.405	0.085	0.418	0.088	0.404	-0.106	0.338	-0.094	0.400	0.087	0.408	0.089	0.397	-0.108	0.330	-0.097	0.383	0.083	0.429	0.085	0.418	
Education																																									
0-11 Years			-0.190	0.001			-0.084	0.125			-0.194	0.001			-0.087	0.116			-0.198	0.001			-0.088	0.107			-0.190	0.001			-0.084	0.128			-0.186	0.001			-0.082	0.133	
12 Years			-0.119	0.008			-0.064	0.127			-0.123	0.007			-0.068	0.109			-0.124	0.006			-0.068	0.105			-0.120	0.007			-0.065	0.118			-0.119	0.008			-0.065	0.122	
13-15 Years			-0.089	0.070			-0.053	0.239			-0.085	0.088			-0.049	0.285			-0.087	0.082			-0.052	0.259			-0.085	0.083			-0.049	0.276			-0.088	0.075			-0.054	0.238	
BMI																																									
Overweight			-0.024	0.560			-0.023	0.549			-0.020	0.629			-0.019	0.621			-0.022	0.594			-0.022	0.579			-0.025	0.552			-0.024	0.545			-0.023	0.574			-0.023	0.556	
Obese 1			-0.038	0.472			-0.043	0.376			-0.031	0.551			-0.036	0.458			-0.033	0.531			-0.039	0.427			-0.035	0.502			-0.040	0.413			-0.036	0.499			-0.042	0.391	
Obese 2			-0.120	0.027			-0.130	0.013			-0.105	0.056			-0.113	0.031			-0.107	0.050			-0.117	0.025			-0.111	0.042			-0.119	0.022			-0.111	0.045			-0.124	0.018	
Smoking																																									
Current Smoker			-0.148	0.002			-0.090	0.078			-0.137	0.004			-0.079	0.127			-0.134	0.005			-0.079	0.125			-0.136	0.004			-0.078	0.130			-0.141	0.004			-0.088	0.093	
Past Smoker			-0.025	0.400			-0.029	0.251			-0.024	0.396			-0.028	0.263			-0.019	0.523			-0.024	0.342			-0.018	0.532			-0.022	0.384			-0.022	0.452			-0.028	0.268	
Alcohol Use																																									
1-4 Drinks per day			0.071	0.008			0.039	0.120			0.071	0.009			0.038	0.136			0.068	0.011			0.035	0.163			0.065	0.014			0.033	0.198			0.068	0.012			0.037	0.148	
5+ Drinks per day			0.030	0.750			-0.106	0.305			0.029	0.763			-0.105	0.324			0.021	0.828			-0.111	0.296			0.032	0.739			-0.104	0.323			0.029	0.759			-0.104	0.323	
CMV Seropositivity																																									
Borderline					-0.101	0.584	-0.087	0.638					-0.109	0.554	-0.095	0.608					-0.100	0.587	-0.086	0.641					-0.099	0.593	-0.086	0.644					-0.100	0.587	-0.088	0.636	
Reactive					-0.645	0.000	-0.633	0.000					-0.643	0.000	-0.630	0.000					-0.641	0.000	-0.629	0.000					-0.643	0.000	-0.631	0.000					-0.643	0.000	-0.632	0.000	
Intercept	2.727	0.000	2.758	0.000	2.567	0.000	2.651	0.000	2.835	0.000	2.863	0.000	2.686	0.000	2.762	0.000	2.779	0.000	2.810	0.000	2.621	0.000	2.704	0.000	2.691	0.000	2.740	0.000	2.553	0.000	2.648	0.000	2.758	0.000	2.785	0.000	2.592	0.000	2.675	0.000	

**Table S6.** Full results for CD4:CD8 ratio.

	I		II		III		IV		V		VI		VII		VIII		IX		X		XI		XII		XIII		XIV		XV		XVI		XVII		XVIII		XIX		XX		
	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p	b	p			
Everyday Discrimination	-0.004	0.839	0.000	0.996	0.011	0.469	0.012	0.461																																	
Stressful Life Events Lifetime Discrimination									-0.011	0.486	-0.014	0.386	-0.007	0.650	-0.009	0.549																									
Life Trauma																																									
Chronic Stress																																									
Age	-0.010	0.000	-0.008	0.000	-0.001	0.532	0.000	0.951	-0.010	0.000	-0.008	0.000	-0.002	0.418	-0.001	0.773	-0.010	0.000	-0.008	0.000	-0.002	0.356	-0.001	0.743	-0.010	0.000	-0.008	0.000	-0.001	0.465	0.000	0.837	-0.011	0.000	-0.008	0.000	-0.002	0.338	-0.001	0.713	
Gender (Female = 1)	0.188	0.000	0.222	0.000	0.272	0.000	0.289	0.000	0.188	0.000	0.221	0.000	0.270	0.000	0.286	0.000	0.179	0.000	0.213	0.000	0.265	0.000	0.282	0.000	0.189	0.000	0.222	0.000	0.270	0.000	0.287	0.000	0.197	0.000	0.229	0.000	0.273	0.000	0.290	0.000	
Race																																									
Black, not Hispanic	-0.261	0.000	-0.226	0.000	-0.001	0.991	0.000	0.993	-0.260	0.000	-0.224	0.000	0.003	0.953	0.002	0.963	-0.242	0.000	-0.206	0.001	0.012	0.812	0.012	0.826	-0.261	0.000	-0.226	0.000	0.001	0.980	0.001	0.992	-0.251	0.000	-0.222	0.000	0.006	0.913	0.003	0.961	
Hispanic	-0.266	0.000	-0.219	0.000	0.036	0.425	0.035	0.475	-0.265	0.000	-0.218	0.000	0.034	0.453	0.033	0.505	-0.265	0.000	-0.216	0.000	0.034	0.459	0.033	0.496	-0.266	0.000	-0.219	0.000	0.034	0.456	0.032	0.513	-0.265	0.000	-0.223	0.000	0.033	0.468	0.030	0.540	
Other, not Hispanic	-0.273	0.007	-0.254	0.010	-0.031	0.727	-0.022	0.801	-0.271	0.007	-0.251	0.011	-0.028	0.754	-0.019	0.833	-0.269	0.008	-0.249	0.012	-0.027	0.757	-0.018	0.835	-0.273	0.007	-0.254	0.010	-0.030	0.737	-0.021	0.808	-0.268	0.008	-0.250	0.012	-0.028	0.753	-0.020	0.825	
Education																																									
0-11 Years			-0.126	0.042			0.011	0.850			-0.128	0.040			0.011	0.848			-0.135	0.029			0.006	0.909			-0.126	0.041			0.012	0.828			-0.118	0.055			0.016	0.784	
12 Years			-0.075	0.108			-0.003	0.940			-0.076	0.104			-0.004	0.925			-0.080	0.092			-0.006	0.884			-0.075	0.109			-0.003	0.940			-0.074	0.118			-0.003	0.944	
13-15 Years			-0.031	0.365			0.016	0.619			-0.030	0.385			0.017	0.599			-0.029	0.406			0.017	0.594			-0.031	0.369			0.015	0.640			-0.027	0.434			0.018	0.576	
BMI																																									
Overweight			0.055	0.187			0.056	0.150			0.056	0.181			0.057	0.145			0.057	0.173			0.058	0.140			0.055	0.186			0.057	0.145			0.057	0.175			0.058	0.139	
Obese 1			0.119	0.031			0.114	0.019			0.120	0.030			0.116	0.019			0.123	0.024			0.117	0.017			0.118	0.031			0.115	0.019			0.123	0.026			0.117	0.017	
Obese 2			0.109	0.031			0.097	0.057			0.112	0.029			0.103	0.044			0.117	0.020			0.106	0.036			0.109	0.035			0.100	0.050			0.126	0.014			0.109	0.032	
Smoking																																									
Current Smoker			-0.144	0.005			-0.071	0.098			-0.142	0.006			-0.068	0.119			-0.132	0.008			-0.063	0.142			-0.145	0.005			-0.071	0.108			-0.127	0.011			-0.061	0.151	
Past Smoker			-0.010	0.781			-0.014	0.629			-0.010	0.778			-0.014	0.650			-0.005	0.896			-0.011	0.724			-0.010	0.765			-0.015	0.625			-0.003	0.930			-0.010	0.733	
Alcohol Use																																									
1-4 Drinks per day			0.120	0.000			0.081	0.010			0.121	0.000			0.080	0.010			0.118	0.000			0.079	0.011			0.121	0.000			0.081	0.010			0.114	0.000			0.077	0.013	
5+ Drinks per day			0.270	0.019			0.096	0.440			0.270	0.020			0.097	0.442			0.260	0.025			0.092	0.465			0.270	0.019			0.097	0.437			0.264	0.023			0.095	0.450	
CMV Seropositivity																																									
Borderline					-0.312	0.037	-0.321	0.035					-0.313	0.038	-0.323	0.036					-0.311	0.040	-0.321	0.038					-0.312	0.037	-0.322	0.035					-0.308	0.039	-0.319	0.036	
Reactive					-0.816	0.000	-0.807	0.000					-0.815	0.000	-0.806	0.000					-0.813	0.000	-0.805	0.000					-0.815	0.000	-0.807	0.000					-0.811	0.000	-0.804	0.000	
Intercept	0.658	0.000	0.422	0.004	0.462	0.001	0.290	0.050	0.675	0.000	0.445	0.003	0.493	0.001	0.321	0.033	0.698	0.000	0.457	0.003	0.504	0.000	0.325	0.030	0.652	0.000	0.426	0.007	0.483	0.001	0.312	0.046	0.706	0.000	0.459	0.002	0.503	0.000	0.324	0.031	

**Table S7.** Correlations among stressor variables.

I	Stressful Life Events	1				
II	Chronic Stress	0.191	1			
III	Everyday Discrimination	0.139	0.368	1		
IV	Lifetime Discrimination	0.281	0.230	0.264	1	
V	Life Trauma	0.096	0.224	0.135	0.245	1
		I	II	III	IV	V

**Table S8.** Principle component analysis among stressor variables.

	PC1	PC2	PC3	PC4	PC5
Stressful Life Events	0.394	0.654	-0.376	0.426	-0.307
Chronic Stress	0.501	-0.396	-0.039	0.519	0.567
Everyday Discrimination	0.463	-0.552	-0.273	-0.246	-0.588
Lifetime Discrimination	0.497	0.314	-0.056	-0.694	0.412
Life Trauma	0.364	0.110	0.883	0.084	-0.262
Eigenvalue	1.883	0.931	0.889	0.706	0.590

Note: all variables were scaled and centered; all components were rotated.

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