Supplementary Materials

Table S1
Standard Deviation and Variance of Inflammation Composite Score by Age Cohort

		T1 Number of chronic health conditions			T2 Number of chronic health conditions		
	n	*M*	*(SD)*	[Var]	*M*	*(SD)*	[Var]
31 to 40 years	105	1.87	(1.97)	[3.87]	1.89	(2.81)	[7.87]
41 to 50 years	267	2.16	(2.39)	[5.73]	4.78	(14.51)	[210.46]
51 to 60 years	298	2.07	(1.93)	[3.72]	3.98	(9.96)	[99.16]
61 to 70 years	196	2.34	(2.11)	[4.44]	4.48	(12.12)	[146.92]
71 to 80 years	73	2.55	(2.32)	[5.36]	5.14	(11.50)	[132.20]
Above 80 years	6	3.00	(2.10)	[4.40]	2.33	(3.08)	[9.47]

Note. *n* = sample size; *M* = mean; *SD* = standard deviation; Var = variance; T1 = time 1; T2 = time 2.

Table S2
Standard Deviation and Variance of Inflammation Composite Score by Gender

		T1 Inflammation Composite			T1 MDD Severity Composite		
	n	*M*	*(SD)*	[Var]	*M*	*(SD)*	[Var]
Female	525	0.07	(0.92)	[0.84]	0.88	(2.04)	[4.18]
Male	420	-0.09	(0.82)	[0.68]	0.37	(1.31)	[1.72]

Note. *n* = sample size; IL-6 = interleukin-6; CRP = C-reactive protein; *SD* = standard deviation; Var = variance; T1 = time 1.

Table S3
Correlations between Moderator Variables

	1	2	3	4	5
1. Age	–				
2. Gender	-0.025	–			
3. Chronic health conditions	0.386***	0.109***	–		
4. Annual household income	-0.075*	-0.303***	-0.106**	–	
5. Frequency of childhood trauma	-0.123***	0.066*	0.160***	-0.065*	–

Table S4
Standard Deviation and Variance of Inflammation Composite Score by Age Cohort

	T1 Inflammation Composite		
	n	*(SD)*	[Var]
31 to 40 years	105	(0.88)	[0.77]
41 to 50 years	267	(0.94)	[0.87]
51 to 60 years	298	(0.85)	[0.72]
61 to 70 years	196	(0.87)	[0.75]
71 to 80 years	73	(0.71)	[0.51]
Above 80 years	6	(0.74)	[0.55]

Note. n = sample size; *SD* = standard deviation; Var = variance; T1 = time 1.

Overall, across age cohorts, the inflammation composite SD and variance steadily decreased with age.

Derivation of Three Inflammation Markers: IL-6, CRP, and Fibrinogen

Within the MIDUS dataset 22 biomarkers were collected of which, only 6 were markers of inflammatory activity: serum IL-6 (pg/mL); serum soluble IL-6 receptor (pg/mL); blood fibrinogen (mg/dl); blood CRP (ug/mL); serum soluble E-selectin (ng/mL); serum soluble intracellular adhesion molecule 1 (ICAM-1) (ng/mL). To determine which inflammatory markers to include we divided the sample in half and as recommended (Matsunaga, 2010; Rosellini & Brown, 2021), a series of factor analyses were performed in the following order: (1) principal components analysis (PCA); (2) exploratory factor analysis (EFA); (3) confirmatory factor analysis (CFA). The dataset was randomly split (Sample 1: $n = 473$; Sample 2: $n = 472$) so that a PCA and EFA was performed on Sample 1, and CFA on Sample 2. EFA was conducted using the *R psych* package (Revelle, 2020).

Exploratory Factor Analysis

PCA used Promax rotation that permitted components to correlate given associations among markers of inflammatory activity. Following the .5/.2 cutoff rule, items with factor loadings ≥ .50 on one component and ≤ .20 on all remaining components were kept. Next, parallel analysis (PA), a conservative and robust item selection approach that facilitated the differentiation of components (Lim & Jahng, 2019), was conducted. A random normal dataset with equal number of participants and variables as the reduced biomarker item pool was generated. Next, this artificially simulated dataset was subjected to factor analyses 1,000 times where eigenvalues for variables were computed through a Jocobi routine (Watkins, 2005). Further, average eigenvalues and standard deviations (SDs) were calculated across replications and juxtaposed with eigenvalues of factors extracted from the original dataset. Factors were retained if the original factor eigenvalue exceeded the average of the parallel factor eigenvalues.

Following this, to ascertain the optimal number of factors to extract to explain the data's variance and to eliminate items that failed to load on any of the extracted factors, EFA with Promax rotation was performed on the reduced item pool together with PA. PA is a reliably precise and best practice approach to factor extraction for continuous variables (Lubbe, 2019). After ascertaining the number of factors, another EFA was conducted, restricted to the number of factors. Similar to PCA, we applied the .5/.2 cutoff rule to keep biomarker items.

PCA of the six inflammation biomarkers in the MIDUS dataset revealed two major components and all biomarkers met the stated .5/.2 cutoff rule (item loadings bolded to increase readability): Component 1 (IL-6: **.76**; CRP: **.81**; fibrinogen: **.82**); Component 2 (serum IL-6 receptor: **.69**; ICAM-1: **.62**; E-selectin: **.60**). EFA was then performed on the six markers. PA steps implied a two-factor solution. However, only three out of six markers of inflammatory activity met the .5/.2 cutoff rule: Factor 1 (IL-6: **.61**; CRP: **.74**; fibrinogen: **.69**); Factor 2 (serum IL-6 receptor: **.47**; E-selectin: **.25**; ICAM-1: **.18**). Therefore, the three markers of inflammatory activity (serum IL-6 receptor, E-selectin, and ICAM-1) in Factor 2 were removed. Another PA and EFA with only IL-6, CRP, and fibrinogen was performed, which suggested a one-factor model (item loadings: IL-6: **.66**; CRP: **.78**; fibrinogen: **.57**).

Confirmatory Factor Analysis

The EFA-derived one-factor solution was validated using CFA. It showed excellent model fit ($\chi^2(df = 1) = 0.090$, $p = .762$, CFI = 1.000, RMSEA = .000). All items loaded highly and significantly (all $p < .001$) on the latent factor (standardized item loadings: IL-6: .612; CRP: .823; fibrinogen: .579). In addition, the mean (or intercepts) (IL-6: 0.679; CRP: 0.312; fibrinogen: 5.792) and residual variances (IL-6: 0.626; CRP: 0.323; fibrinogen: 0.665; latent inflammatory activity composite: 1.000) were all statistically significant (all $p < .001$).

References

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