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A novel approach to model cumulative stress: Area under the s-factor curve

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A R T I C L E I N F O

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A B S T R A C T

Objective: Using a large longitudinal sample of adults from the Midlife in the United States (MIDUS) study, the present study extended a recently developed hierarchical model to determine how best to model the accumulation of stressors, and to determine whether the rate of change in stressors or traditional composite scores of stressors are stronger predictors of health outcomes.
Method: We used factor analysis to estimate a stress-factor score and then, to operationalize the accumulation of stressors we examined five approaches to aggregating information about repeated exposures to multiple stressors. The predictive validity of these approaches was then assessed in relation to different health outcomes.
Results: The prediction of chronic conditions, body mass index, difficulty with activities of daily living, executive function, and episodic memory later in life was strongest when the accumulation of stressors was modeled using total area under the curve (AUC) of estimated factor scores, compared to composite scores that have traditionally been used in studies of cumulative stress, as well as linear rates of change.
Conclusions: Like endogenous, biological markers of stress reactivity, AUC for individual trajectories of self-reported stressors shows promise as a data reduction technique to model the accumulation of stressors in longitudinal studies. Overall, our results indicate that considering different quantitative models is critical to understanding the sequelae and predictive power of psychosocial stressors from midlife to late adulthood.

A Novel Approach to Model Cumulative Stress: Area Under the s-factor Curve Environmental and psychosocial stressors predict a wide range of physical and mental health outcomes (Schneiderman et al., 2005). The deleterious effects of exposure to multiple stressors and repeated exposures to any stressor are believed to increase the health detriments of any single exposure (Mann et al., 2021). Yet, modeling the accumulation of stressors over time remains an outstanding challenge for social epidemiology, as there is little to no consensus on how to best capture individual differences in cumulative stress (Mann et al., 2021). The optimal number of stressors, the relative importance of different dimensions of stressors at different life stages, and the best way to model simultaneous and repeated exposures remain unresolved.

To date, many studies of the links between stressors and health have focused on exposure to a single psychosocial stressor during a specific period of development, such as early life, mid-life, and older adulthood. For example, studies have focused on the impact of relationship strain

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(Walen et al., 2000), daily discrimination (Williams et al., 1997), and work-family spillover (Grzywacz et al., 2000). This type of study design is invaluable because it provides a focused and fine-grained examination of the relationship between a specific stressor and outcome. However, it is neither well suited for capturing the multidimensionality of psychosocial stressors, the tendency for multiple stressors to co-occur, nor the accumulation of repeated stressors over time-i.e., *cumulative stress.* Indeed, one stressor is rarely experienced in isolation. Rather, stressors typically co-occur in individuals' lives, particularly for racially minoritized groups (Mann et al., 2021). Consequently, measuring cumulative stress is particularly challenging because it involves the aggregation of information about many different variables that are contingent upon and change over time. Indeed, measuring the exposome—the totality of pathogenic exposures over the life course—a concept that shares a family resemblance to cumulative stress, has been described as an outstanding challenge of epidemiology (Wild, 2005).

Historically, empirical studies that have examined the association between cumulative stress and health have relied on a unit-weighted composite score or cumulative risk index to model cumulative stress using self-report measures (Sternthal et al., 2011; Brewer et al., 2018; Puterman et al., 2016; Lampert et al., 2016; Slopen et al., 2012, 2013; Evans et al., 2013a, 2013b). Most often, composite scores are created by standardizing individual measures of stressors, calculating a sum score of the standardized measures, and then standardizing the resulting sum score (Sternthal et al., 2011; Brewer et al., 2018; Puterman et al., 2016; Lampert et al., 2016; Burroughs Peña et al., 2019; Slopen et al., 2018; Albert et al., 2017). Alternatively, binary stressors are simply counted, or continuous stressor are dichotomized and then counted to create a cumulative risk index (Evans et al., 2013a). Advantages of this approach include simple and parsimonious modeling, prediction of health outcomes, and purported ease of interpretation for the general public and health officials (Mann et al., 2021). However, unit-weighted composite scores also have disadvantages, including the assumptions that stressors are unidimensional and different stressors contribute equally to the accumulation of stressors.

As a first step to help improve the operational definition of cumulative stress using secondary data, Burchinal and colleagues (Burchinal et al., 2000) compared different approaches to operationalize cumulative social risk in relation to cognitive development in childhood. The authors compared the effects of individual stressors, factor scores derived from individual stressors, and a cumulative risk index that was a sum of the total number of stressors. Comparing multiple regression coefficients, the effects of factor scores were most often statistically significant and tended to be larger in size than individual stressors and the sum score of dichotomized stressors. The authors concluded that "use of individual risk variables provides better overall prediction of developmental outcomes at a particular age but is less useful in predicting developmental patterns. The risk factor (score) approach provides good prediction of developmental trajectories when sample sizes are moderate to large. Finally, the risk index approach is useful for relating social risk to developmental patterns when a large number of risk variables are assessed with a small sample" (Burchinal et al., 2000). Although this work makes an invaluable contribution to optimizing the operational definition of cumulative stress using secondary data, the study was small ($n = 87$), lacked racial diversity, and focused exclusively on cognitive outcomes in early childhood, which limits the generalizability of findings.

Extending this important work, Mann et al. (2021) used factor analytic techniques to derive an empirically grounded, hierarchical model of stressors based on the patterns of correlations among a large battery of psychosocial stressors. In contrast to unit-weighted sum scores of multiple stressors, or a mean standardized composite score, this approach captures the multidimensional structure of cumulative stress, accounts for unsystematic measurement error, and differentially weights individual stressors to reflect the fact that not all stressors contribute equally to the likelihood of experiencing multiple stressors. Indeed, the tendency for multiple dimensions of psychosocial stressors to correlate was captured by a general higher-order factor, coined the "s-factor" of stress (Mann et al., 2021).

Building from these studies, the present study estimates intra-individual changes in s-factor scores using three waves of data, spanning approximately two decades, to model inter-individual differences in cumulative stress over time. Moreover, we test a novel application of an analytic technique to model individual differences in repeated exposure to stressors over time and compare this technique to composite scores that have been used in past studies to model cumulative stress. Finding this novel application to outperform traditional composite scores of cumulative stressors might benefit future studies' prediction of health outcomes.

1. Area under the curve

There are analytic techniques used in neuroendocrinology to model physiological markers of stress, usually cortisol, and individual differences in stress reactivity. Area under the curve with respect to ground (AUC_G, i.e., total AUC) and area under the curve regarding increase (AUC_I) are often used in neuroendocrinology to capture diurnal patterns of cortisol, as well as cortisol reactivity to laboratory stressors (Fekedulegn et al., 2007; Pruessner et al., 2003). Simply put, AUC captures the total amount of a variable that has been observed over a temporal period or observational "window", irrespective of whether the variable increases, decreases, fluctuates, or remains stable over time. Here, we use AUC to model cumulative exposure to psychosocial stressors over time, and we test whether AUC outperforms traditional composite scores of stressors (Sternthal et al., 2011; Evans et al., 2013b) and linear slopes of stressors in the prediction of health outcomes. Given that AUC has been used to measure stress reactivity beneath the skin, we evaluate whether AUC can be used to measure the accumulation of psychosocial stressors outside the skin.

AUC_G calculates the total area under the curve for repeated measurements, taking into account change over time and the distance of the repeated measures from zero (i.e., the absolute level of stressors) (Fekedulegn et al., 2007; Pruessner et al., 2003). AUC_G is depicted for a hypothetical trajectory of cumulative stress in panel A of Fig. 1. The trajectory is characterized by an increase from the first measurement to the second, and again by an even more rapid increase from the second measurement to the third. On the other hand, the trajectory in panel B is characterized by an increase from the first measurement to the second, followed by a decrease from the second measurement to the third. Note, the average rate of change is greater for the trajectory depicted in Panel A, compared to Panel B. However, if AUC_G were calculated for the trajectory in Panel B, then it would be greater than AUC_G for the trajectory in panel A, because AUC_G incorporates information about the initial level, as well as the rate and direction of change.

In contrast to AUC_G, area under the curve regarding increase (AUC_I) places greater emphasis on the rate of change, as it subtracts out the level of stress at the first measurement from the area under the curve. AUC_I is depicted for the hypothetical trajectory of cumulative stress depicted in panel B. As the initial level of stress, or the distance from the "ground" or "base" of the y-axis, is subtracted from the area when calculating AUC_I, the rank-order of AUC_I for the two trajectories (A & B) has changed relative to AUC_G, such that AUC_I is greater for the trajectory depicted in panel A, compared to the trajectory depicted in panel B. Consequently, AUC_G and AUC_I might be expected to exhibit differential prediction of health-related outcomes.

For example, if the initial or absolute level of cumulative stress is particularly relevant to the etiology or pathogenesis of a health outcome, in addition to the rate of change over time, then the predictive potency of AUC_G should exceed that of a unit-weighted composite score (depicted in panel C of Fig. 1), a linear slope (depicted in panel D of Fig. 1), or AUC_I, because AUC_G is the only measure that incorporates information about both the initial-level and rate of change. Similarly, if

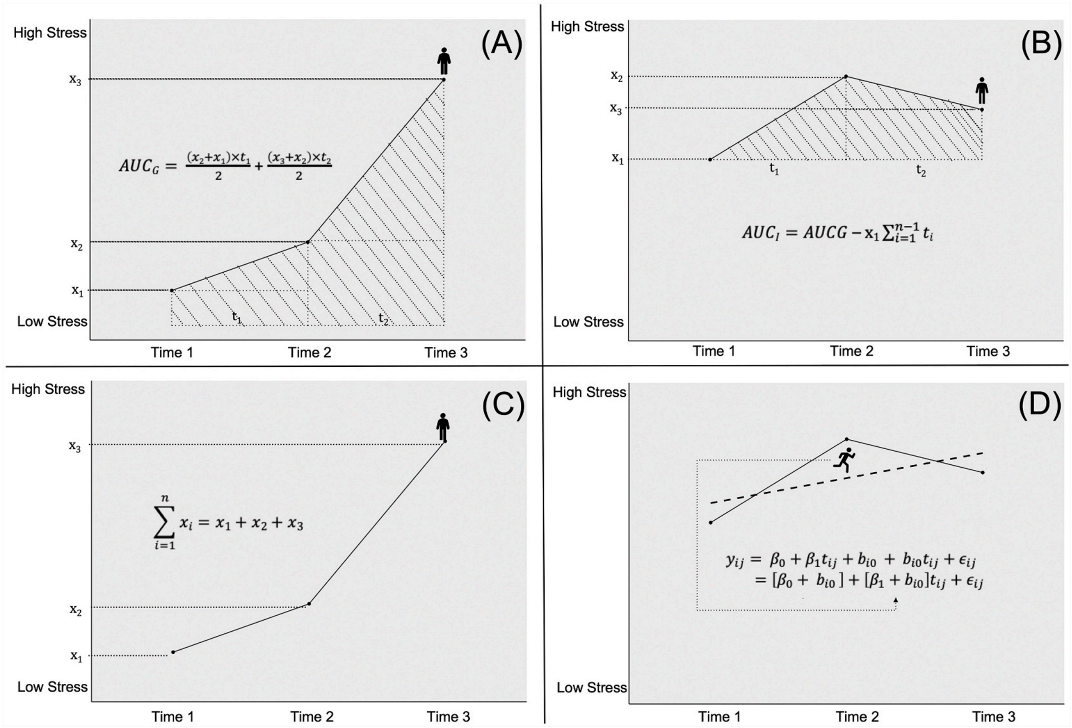

Fig. 1. Different Longitudinal Approaches to Model Cumulative Stress
Notes. Panel A depicts area under the curve with respect to ground (AUC_G). Panel B depicts area under the curve with respect to increase (AUC_I). Panel C depicts a unit-weighted sum score. Panel D depicts a linear slope. $x_1 - x_3$ = measurements of stress at three waves of data collection. $t_1 - t_2$ = time intervals between measurements of stress.

there is little change in a stressor over time or persistent stable exposure is especially relevant to a health outcome, then the predictive potency of AUC_G should again exceed that of AUC_I or linear slopes. On the other hand, if individuals adapt, habituate, or become inured to the typical levels of stress in their lives, and changes in stressors over time are more relevant to a health outcome, then the predictive potency of AUC_I or linear slopes (capturing individual rates of change) should exceed AUC_G. Finally, if the relevant change in stressors is curvilinear or non-monotonic, then the predictive potency of AUC_I should outperform linear slopes, which fail to adequately capture departures from linearity.

2. Goals of the present study

The present study tests whether two distinct measures of area under the curve for higher-order and lower-order dimensions of cumulative stress outperform traditional composite scores and linear slopes of stressors in the prediction of health outcomes. After determining the optimal approach to model cumulative stress over time, as indicated by the strongest predictor of health outcomes, we test the relative contributions of demographic factors and cumulative stress to the variance explained in health outcomes at different ages. Thus, the present study aims to shed light on whether AUC is an adequate means of modeling the accumulation of stressors over time, while also estimating the relative predictive power of demographic factors versus cumulative stress in relation to physical and cognitive health outcomes at different life stages, specifically across early-to-middle and middle-to-late adulthood.

3. Method

3.1. Sample

The analytic sample ($n = 6397$) came from the Midlife Development in the United States (MIDUS) study (Ryff et al., 2018), which is publicly available to interested investigators via the MIDUS Colectica portal (http://midus.colectica.org), including data from the MIDUS-I, MIDUS-II, and MIDUS-III waves of data collection. Data collection was conducted from 1995 to 1996 for MIDUS-I, 2004–2005 for MIDUS-II, and 2013–2014 for MIDUS-III. The analytic sample includes adults (range of ages = 20–75 years at baseline), male and female (54%), who predominately identified as White race/ethnicity (~88%) and reported considerable variability in educational attainment (e.g., ~28% of the sample graduated from high school and did not attend college, while ~18% completed a bachelor's degree). Analytic sample sizes and sample characteristics at each wave of data collection are reported in Table 1.

3.2. Measures

Descriptive statistics for study variables are reported in supplemental material (Table S1). Detailed descriptions of study variables can be found in MIDUS study documentation. Demographic factors included chronological age (in years), self-reported sex (female or male), self-reported level of education, and self-reported race/ethnicity (White, Black, Native American, Asian or Pacific Islander, and Other Race/Ethnicity). Because few participants self-identified as Native American (~1%), Asian or Pacific Islander (~1%), or other race/ethnicity (~2%), these racial/ethnic categories were combined into a single variable, titled "Other race/ethnicity".

Health Outcomes. Four physical health outcomes at the final wave of data collection were included in the analyses: self-reported number of physical conditions, body mass index (BMI), basic activities of daily living (e.g., "Bathing or dressing yourself"), and intermediate or moderate activities of daily living (e.g., "running or lifting heavy objects"). Activities of daily living were coded such that higher values reflect greater difficulty completing activities. Two cognitive health outcomes at the final wave of data collection were included in the analyses: executive function and episodic memory scores from the Brief Test of Adult Cognition by Telephone (BTACT) (Lachman et al., 2014).

Stressors. Nineteen self-reported measures were included in

Table 1
Sample characteristics.

	MIDUS-I (n = 6397)		MIDUS-II (n = 4784)		MIDUS-III (n = 3249)	
	M/f	*SD/%*	*M/f*	*SD/%*	*M/f*	*SD/%*
Age	46.79	12.89	55.62	12.40	63.70	11.34
Sex						
Female	3362	53%	2572	54%	1792	55%
Male	3035	47%	2212	46%	1457	45%
Race/Ethnicity						
White	5622	88%	4346	91%	2886	89%
Black/African American	322	5%	195	4%	116	4%
Native American	39	1%	73	2%	28	1%
Asian or Pacific Islander	57	1%	31	1%	13	<1%
Other	174	2%	117	2%	180	6%
Missing	183	3%	22	<1%	26	<1%
Educational Attainment						
None/Some Grade School	27	<1%	13	<1%	6	<1%
8th Grade/Junior High	99	2%	62	1%	25	1%
Some High School	436	7%	221	5%	136	4%
GED	92	1%	58	1%	32	1%
High School Diploma	1750	27%	1216	25%	741	23%
1–2 Years College	1168	18%	852	18%	498	15%
>2 Years College	290	5%	201	4%	104	3%
Associate degree	484	8%	373	8%	336	10%
Bachelor's Degree	1159	18%	928	19%	711	22%
Some Graduate School	180	3%	148	3%	74	2%
Master's Degree	460	7%	483	10%	405	12%
Ph.D., J.D., M.D.	239	4%	223	5%	170	5%
Missing	13	<1%	6	<1%	11	<1%

Notes. n = sample size. M = mean. f = frequency. SD = standard deviation. % = percentage.

analyses, which included indicators of economic and racial disadvantage, stressors related to home, work, and interpersonal relationships: (1) daily discrimination, (2) lifetime discrimination, (3) lack of coworker support, (4) lack of supervisor support, (5) high job demands, (6) risk of accident or injury at work, (7) work-family spillover, (8) family-work spillover, (9) inequality at work, (10) inequality with family, (11) inequality at home, (12) poor neighborhood quality, (13) family strain, (14) friendship strain, (15) spouse strain, (16) marital risk, (17) not enough money to meet one's needs, (18) difficulty paying monthly bills, and (19) a subjective assessment of one's current financial situation. The number of items for each scale, item content, coding and scaling schemes can be found in supplemental materials. Note, the reference period is not the same for all the measures of stressors, and this is neither a prerequisite for estimating factor scores nor calculating area under the curve of estimated factor scores. Whether respondents report "How many times in your life" or "How often on a day-to-day basis" they experience a stressor, that stressor has the potential to repeat over time and result in cumulative effects on health.

3.3. Data analysis

Data were imported into R Studio version 3.1.1056 (Allaire, 2012), processed, and then exported using the 'MplusAutomation' package version 0.7.1 (Hallquist et al., 2018). Analyses were conducted using Mplus version 8.1 (Muthén et al., 2017) and using the 'rwa' and 'lavaan' packages (Chan, 2020; Rosseel, 2012) in R Studio. Figures were created using the 'ggplot2' package (Wickham et al., 2016). Based on the hierarchical model reported by Mann et al. (2021), the confirmatory factor analysis (CFA) model depicted in Fig. 2 was specified at each wave of data collection. To reflect strict longitudinal measurement invariance, the factor loadings, variance of the cumulative s-factor, and the residual variances of lower-order factors were constrained to equality across measurements, as were the intercepts and residual variances of individual indicators. To help prevent the inflation of latent variable correlations, same-variable cross-time residual correlations were included and constrained to equality across measurement occasions (Grimm et al., 2010). The model was estimated using maximum likelihood with robust standard errors (MLR), adjusting estimates for the non-independence of observations that results from relatives being nested within the same family using the CLUSTER option coupled with a family identification number (Muthén et al., 2017). Next, the parameter constraints described above were freed in a series of models to test for longitudinal measurement invariance, with successive models compared using change in model chi-square rescaled to a RMSEA metric (i.e., root deterioration per restriction) (Hildebrandt et al., 2009), change in root mean squared error of approximation (ΔRMSEA) (Chen, 2007; Cheung et al., 2002), and change in comparative fit index (ΔCFI) (Chen, 2007; Cheung et al., 2002).

Before calculating the AUC of estimated factor scores, a series of factor of curves models (McArdle et al., 1987) with individually varying times of observation (Grimm et al., 2016) were estimated to obtain subject-specific linear slopes for each dimension of cumulative stress. In these models, the factor loadings of latent slopes were fixed to equal the age of participants (in years) at each measurement occasion, and the variances and covariance of growth factors were freely estimated. Individual differences in slopes were then estimated and saved for comparison to AUC_G and AUC_I in the prediction of health outcomes across dimensions of cumulative stress. For all models, the default setting in MPlus was used for dependent variables with missing data, which is full information maximum likelihood. Details on calculating factor scores can be found elsewhere (Grice, 2001) and obtained easily using the 'psych' package in R (Revelle et al., 2015).

3.3.1. Traditional composite scores of cumulative stress

Following the procedures that have been used in past studies of cumulative stress (Sternthal et al., 2011; Brewer et al., 2018; Puterman et al., 2016; Lampert et al., 2016; Slopen et al., 2012, 2013), a composite score was created by standardizing each measure of stress based on the mean and variance at the first wave of data collection, summing all standardized measures that are indicators of a given dimension of stress, and then standardizing ($M = 0$, $SD = 1$) the resulting summary score. A dichotomized version of the standardized summary score was also calculated, such that scores in the top quintile were contrasted with scores in the lower quintiles. Studies of cumulative stress have traditionally used the top-quintile threshold based on research that indicates the effects of stressors are most salient among those experiencing severe stressors (Williams et al., 2009), with sensitivity analyses revealing similar results when the threshold is determined using the top-tercile or top-quartile (Sternthal et al., 2011).

Next, to place even greater emphasis on the most severe stressors, a sum of dichotomized stressors was computed for each dimension of stress (i.e., a cumulative risk index). First, continuous scores for measures of psychosocial stress were divided into deciles and dichotomized, such that the stressor was coded as having occurred if the continuous score was among the top 10% of scores, while the stressor was coded as having not occurred if it was among the lower 90% of scores. For stressors measured by a single item rated on a Likert scale, the stressor was coded as having occurred if the highest response category was endorsed, and the stressor was coded as having not occurred for all other response categories. A unit-weighted sum score was then calculated among the resulting binary stressors (0 = did not occur, 1 = occurred)

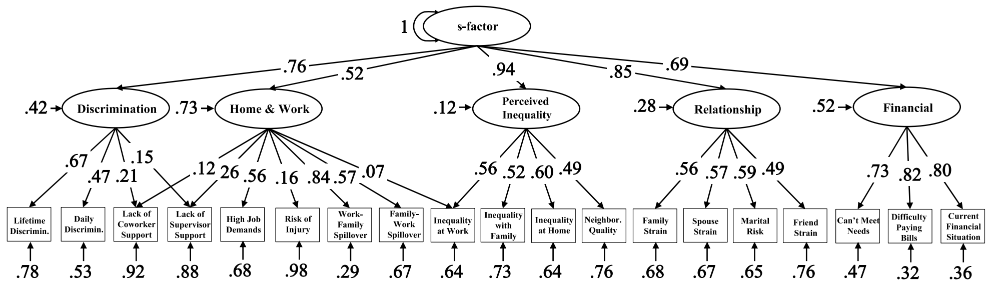

Fig. 2. Standardized Estimates for the Hierarchical Model of Stress
Notes. Parameter estimates were constrained to equality across the three measurement occasions. Test-retest correlation for s-factor = 0.89. All estimates are statistically significant at $p < 0.001$.

for each dimension of stress based on the configuration of factor indicators depicted in Fig. 2.[1] To facilitate comparison with the dichotomized version of the standardized summary score, a dichotomized version of the resulting cumulative risk index was also calculated based on the upper vs. lower quintiles.

3.3.2. Area under the curve

Using the formulas reported in Fig. 1, AUC_G and AUC_I were calculated for the individual trajectories of factor scores depicted in Fig. 3. Before calculating AUC, factor scores were standardized using the mean and variance of the respective scores at wave 1. Next, to ensure the calculation of true areas for AUC_G (Fekedulegn et al., 2007; Pruessner et al., 2003), factor scores were centered to redefine zero as the lowest observed score on each dimension of cumulative stress. Details and worked examples for calculating AUC_G and AUC_I can be found elsewhere (Fekedulegn et al., 2007). Again, to facilitate the comparison of effect size estimates, dichotomized versions of AUC_G and AUC_I were calculated based on the upper vs. lower quantiles of the respective scores. In Fig. 3, the solid black lines are trajectories of psychosocial stressors for individual participants, and the dashed gray lines denote the loess curves (Cleveland et al., 1988) with 95% confidence bands shaded in orange. These plots are depictions of the trajectories of stress for which AUC_G and AUC_I were calculated.

3.3.3. Prediction of health outcomes

Next, a series of multiple regressions were estimated to assess the relative strength of the scores described above to predict health outcomes. In each model, either number of chronic conditions, body mass index (BMI), intermediate or basic activities of daily living, executive function, or episodic memory were specified as the criterion, predicted by either AUC_G, AUC_I, the traditional standardized summary score, the unit-weighted sum of dichotomized stressors (i.e., cumulative risk index), or random slopes for a dimension of stress. The resulting standardized regression coefficients are interpreted as the predicted change in the outcome (increase or decrease) in standard deviation units given a standard deviation increase in the composite measure of psychosocial stressors. The same multiple regressions were then estimated with the corresponding dichotomized scores based on upper vs. lower quantiles.

Because these scores are different interrelated ways of aggregating information about the same set of stressors, these scores were not included in a regression as simultaneous predictors. Instead, each of the five predictors were included, one at a time, in a series of successive models. Multiple regression models also included age at baseline, sex (0 = female, 1 = male), level of education, black race (0 = No, 1 = Yes), and other race (0 = No, 1 = Yes), with the largest group as the reference category (White). The effects of focal predictors are, thus, adjusted for the effects of the demographic variables noted above. This analytic process resulted in the estimation of 360 multiple regressions (5 longitudinal stress scores × 2 continuous and binary versions based on the upper vs. lower quantiles × 6 dimensions of stress × 6 health outcomes). Consequently, we did not interpret null hypothesis significance tests of individual regression parameters because family-wise error would greatly increase the likelihood of false positives. Therefore, we chose to interpret only the size and overall pattern of parameter estimates by plotting standardized regression coefficients with 95% confidence intervals.

As the strength of different predictors could vary across dimensions of stress and stages of adulthood, we first examined the pattern of results from multiple regressions to identify the strongest of the predictors for each health outcome and each dimension of stress. Next, given the associations between demographic factors and health outcomes, as well as demographic differences in cumulative stress, we also estimated the *unique* contribution of demographic factors and cumulative stress to the explained variance in health outcomes using relative weights analysis (Johnson, 2000; Wright et al., 2017). To adjust for the correlations among predictors in a multiple regression, relative weights analysis applies a transformation to each predictor to create a new set of orthogonal predictors "that are maximally similar to the original variables" (Johnson, 2000). To assess whether the impact of each dimension of stress varied across stages of adulthood, relative weights analysis was stratified across age groups at baseline, which were defined by decade (e.g., 40s, 50s, 60s, etc.). Again, due to the number of tests (6 health outcomes × 6 predictors (demographic factors + cumulative stress) × 5 age groups = 180 regression coefficients), the binary decision to accept or reject a null hypothesis was bypassed by focusing on effect size estimates in the interpretation of results, specifically the relative contributions of variables to the explained variance in health outcomes.

4. Results

4.1. Factor analysis models

Model chi-square ($\chi 2$), root mean squared error of approximation (*RMSEA*), and comparative fit index (*CFI*) evinced acceptable fit to the data for the model depicted in Fig. 2 (model $\chi 2 = 11826.91$, $df = 1619$, p

[1] The traditional composite scores (standardized summary score and sum score of dichotomized stressors) corresponding to the s-factor included all 19 stressors across the three waves of data collection. The composite scores for discrimination included 4 stressors (daily discrimination, lifetime discrimination, lack of co-worker support, and lack of supervisor support). The composite scores for home and work-related stress included 6 stressors (high job demands, lack of co-worker support, lack of supervisor support, negative work-family spillover, and negative family-work spillover). The composite scores for inequality included 4 stressors (neighborhood quality, inequality at home, inequality with family, and inequality with friends). The composite scores for relationship stress included 4 stressors (family strain, friendship strain, spousal strain, and marital risk). Finally, the composite scores for financial stress included 3 stressors (not enough money to meet one's needs, difficulty paying bills, and current financial situation)..

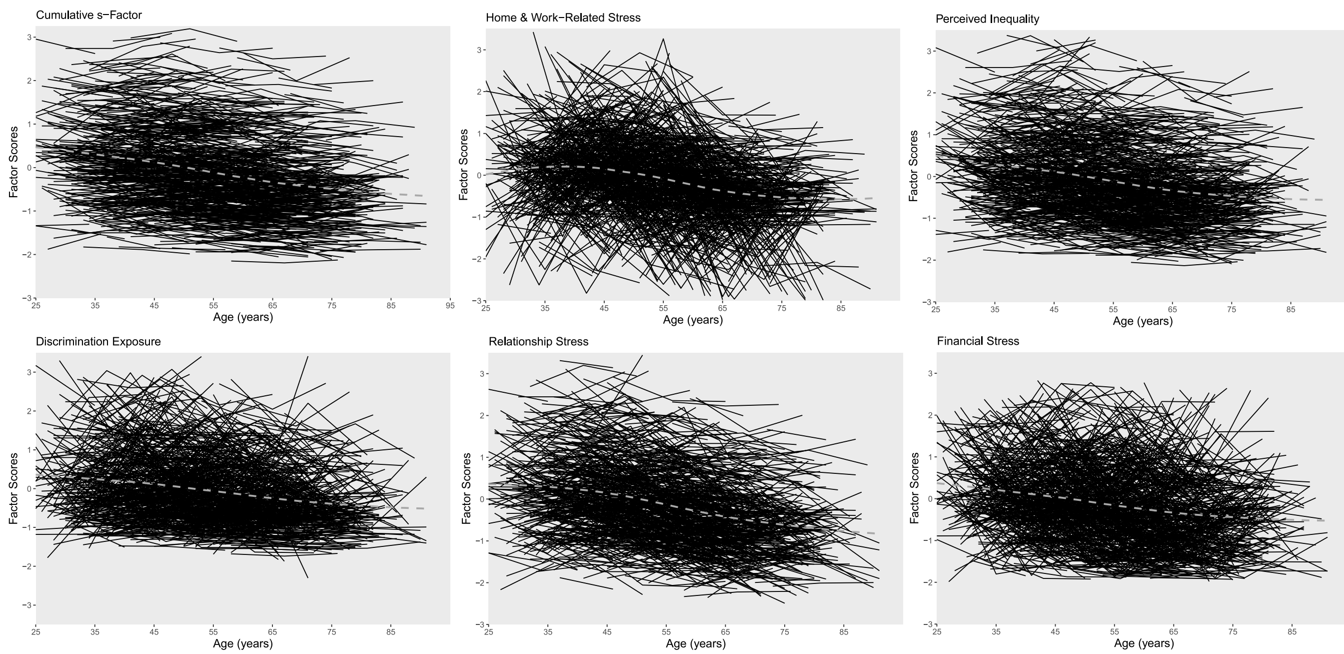

Fig. 3. Individual Trajectory Plots for Different Dimensions of Stress
Notes. Y-axis = estimated factor scores across 3 waves of data standardized using the mean and standard deviation at wave 1. X-axis = chronological age. Each black line depicts a trajectory of stress for a participant. The gray dashed line and orange shaded region in each panel depicts the best-fitting loess trend with 95% confidence intervals.

< 0.001, *RMSEA* = 0.031, *CFI* = 0.851). Although CFI fell below the traditional threshold for good fit (*CFI* > 0.90), as noted elsewhere (Mann et al., 2020), *RMSEA* may be preferred over *CFI* "in confirmatory contexts, when researchers wish to determine whether a given model fits well enough to yield interpretable parameters" (Rigdon, 1996). Factor determinacy was high for the cumulative s-factor (average *FDI* = 0.91) and adequate-to-high for subordinate dimensions of stress (range of *FDI* = [0.82, 0.92]). Results of model comparisons are reported in supplemental material, which provided mixed support for longitudinal measurement invariance (Table S2). However, absolute fit statistics and FDIs were similar after freely estimating potentially non-invariant parameters across the three waves of data collection (range of *FDI* = [0.84, 0.92]), suggesting the impact of potentially non-invariant parameters had little influence on the calculation of factor scores. Consistent with these findings, the factor scores from the fully invariant model were almost perfectly correlated ($r = 0.99$) with the factor scores from unconstrained models. Therefore, factor scores from the model depicted in Fig. 2 were saved for subsequent analyses.

4.2. *Trajectories and measures of stress*

The temporal stability of the cumulative s-factor is visually evident, as many of the individual trajectories in Fig. 3 appear approximately flat, particularly for the s-factor and the subordinate dimension of stress with the strongest loading on the s-factor, namely, perceived inequality. This is consistent with the high retest correlation that was observed for the s-factor in the hierarchical model depicted in Fig. 2 ($r = 0.89$, $p < 0.001$). Nevertheless, the averages of linear slopes from curves of factors models were negative and statistically significant across all dimensions of cumulative stress (p-values <0.001), and there was significant variance in initial-levels and rates of linear change (p-values <0.001). The loess curves depicted in Fig. 3 confirmed these negative age-related trends, such that average levels of stress tended to decrease from early to late adulthood. The distributions of AUC_G and AUC_I for individual trajectories of cumulative stress are depicted using histograms in supplemental material (Fig. S1). Distributions of AUC_I and the mean standardized composite scores were approximately Gaussian, and distributions of AUC_G exhibited slight positive skew. On the other hand, distributions of the cumulative risk index were zero-inflated and highly skewed. Correlations between AUC_G for different dimensions of stress were moderate to large (mean $r = 0.83$, range = [0.45, 0.98]), correlations between AUC_I were small to large (mean $r = 0.35$, range = [0.08, 0.90]) and correlations between AUC_G and AUC_I were comparatively small (mean $|r| = 0.05$, range = [-0.08, 0.12]).

4.3. *Prediction of health outcomes*

Results of multiple regressions are depicted in Fig. 4 and reported comprehensively in supplemental material (Table S3), including multiple regressions that used full information maximum likelihood and listwise deletion of missing values. Comparing the predictive strength of different approaches to model cumulative stress, AUC_G consistently had the largest multiple regression coefficient irrespective of the dimension of stress or physical health outcome. The second strongest estimate was the traditional composite score, followed by the unit-weighted sum score of dichotomized stressors, $AUC_{I,}$ and slopes. Crucially, on average, there was a 104% increase in the standardized regression coefficient of AUC_G compared to the standardized summary score approach that has been used in past studies to model the accumulation of stressors (mean = 104.59%, median = 89.13%, minimum = 41.23%, maximum = 320.91%). When comparing the predictive strength of binary predictors based on the upper and lower quintiles of their continuous counterparts, the same pattern of results emerged. These results are depicted in supplemental material (Fig. S2). AUC_G was the strongest predictor of physical and mental health outcomes, followed by the traditional summary score, the sum of dichotomized stressors, AUC_I and linear slopes. Compared to the upper quintile of the standardized composite score that has commonly been used in studies of cumulative stress, on average, the standardized regression coefficient increased by 138% for the upper quartile of AUC_G (mean = 138.72%, median = 94.44%, minimum = 3.40%, maximum = 1469.81%). Consequently, AUC_G was selected as the preferred approach to model cumulative stress and was carried forward to subsequent analyses.

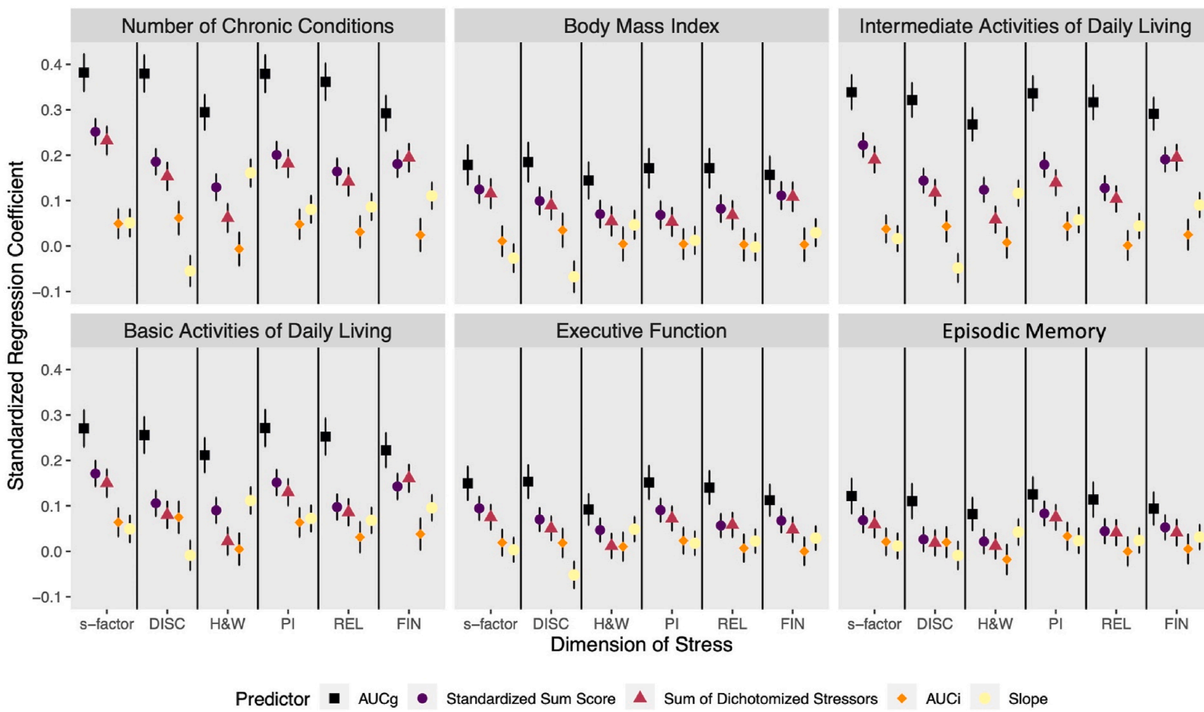

Fig. 4. Prediction of Physical and Cognitive Health Outcomes by Different Summary Scores Across Different Dimensions of Cumulative Stress
Notes. Y-axis = standardized multiple regression coefficient adjusted for the effects of age, sex, race, and level of education. Positive regression coefficients are associated with worse health outcomes, i.e., more chronic conditions, higher BMI, greater difficulty completing activities of daily living, and lower executive function and episodic memory. X-axis = dimensions of cumulative stress: DISC = discrimination. H&W = home & work-related stress. PI = perceived inequality. REL = relationship stress. FIN = financial stress. Vertical lines denote 95% confidence intervals. AUC_G = area under the curve with respect to ground, a. k.a. total area under the curve. AUC_I = area under the curve regarding increase.

4.4. Contributions to explained variance in health outcomes

The effects of demographic factors on cumulative stress are depicted in Fig. 5 and comprehensively in supplemental material (Table S4). The results of relative weights analysis are depicted in Fig. 6 and comprehensively in supplemental material (Table S5). The relationships between demographic factors and different dimensions of cumulative stress are in the expected directions. For example, across dimensions of

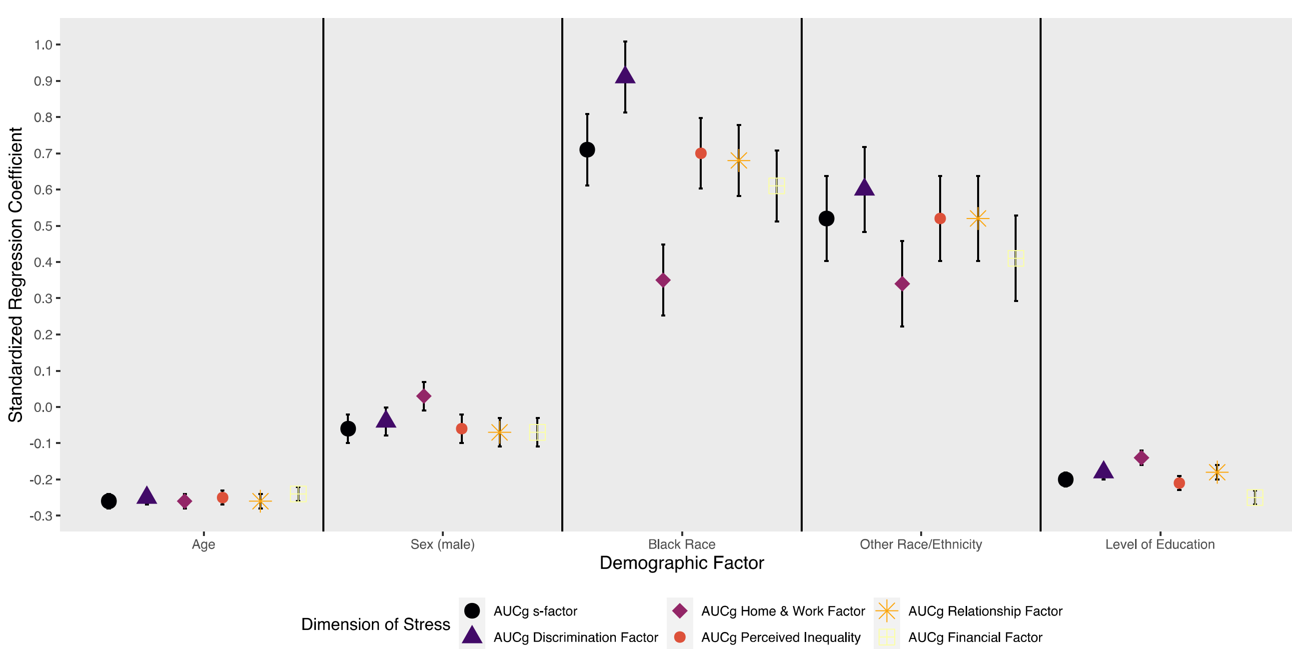

Fig. 5. Effects of Demographic Factors on Different Dimensions of Cumulative Stress Modeled Using Area Under the Curve with Respect to Ground (AUC_G)
Notes. Y-axis = standardized multiple regression coefficient reporting or adjusted for the effects of age, sex (0 = male, 1 = female), black race (0 = No, 1 = Yes), other race (0 = No, 1 = Yes; Reference = White), and level of education. X-axis = Demographic factor. Positive regression coefficients are associated with higher cumulative stress. Vertical lines denote 95% confidence intervals.

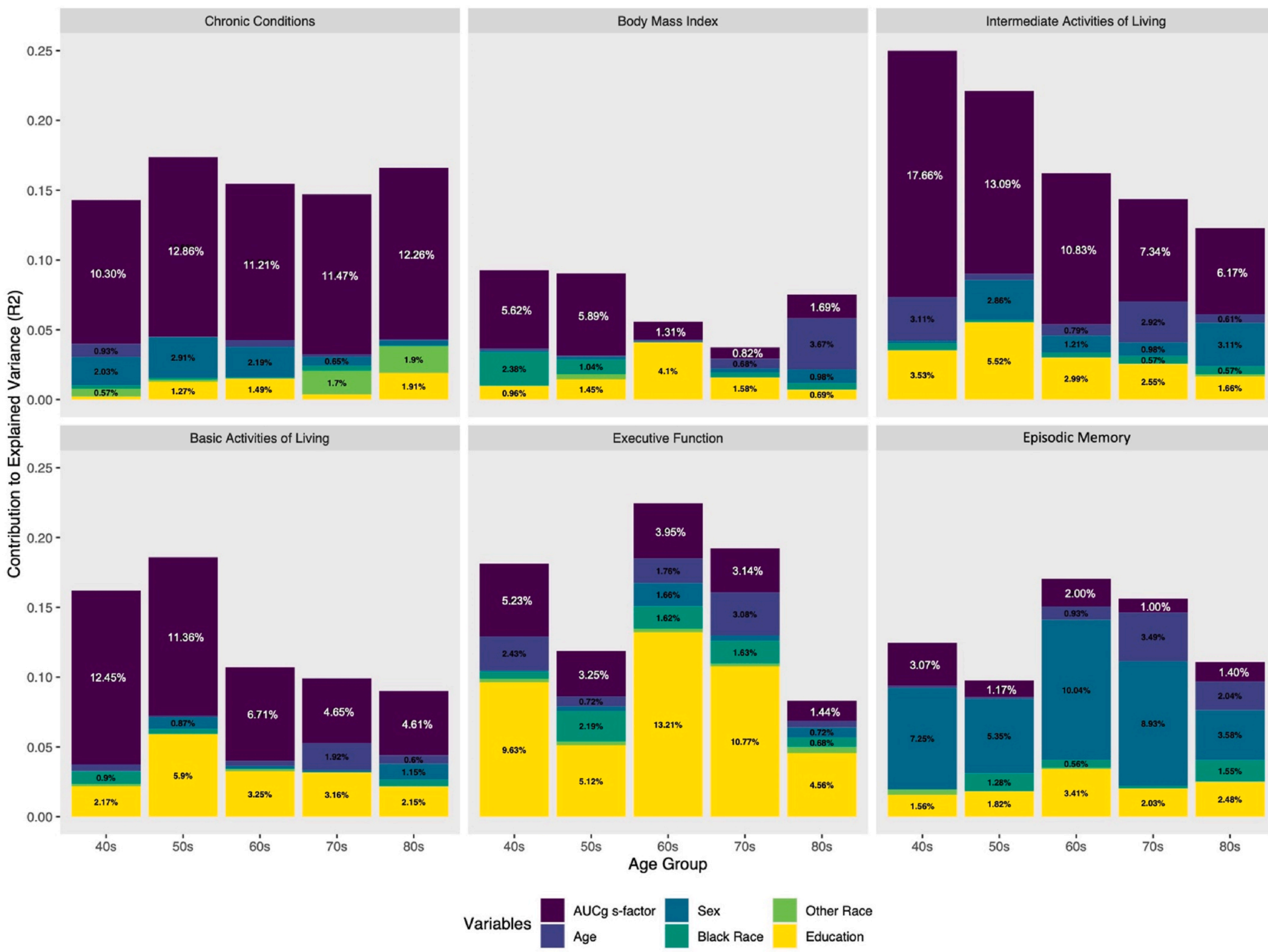

Fig. 6. Relative Weights of Demographic Factors and Area Under the Curve of the s-factor for Dimensions of Stress Predicting Physical and Cognitive Health Outcomes

Notes. Results of relative weights analysis are plotted for health outcomes across different age groups. Variables with contributions to R^2 that did not exceed 0.50% are not annotated with text to ease visualization.

stress, older age and higher levels of education were associated with lower levels of stress, while being Black or another non-White race/ethnicity was associated with higher levels of stress. Being male, as opposed to female, was associated with slightly lower levels of cumulative stress, except for home and work-related stress. Moreover, the effect of being black, compared to white, was especially pronounced for the dimension of stress related to interpersonal experiences of discrimination (e.g., daily discrimination, lifetime discrimination, lack of supervisor support, and lack of coworker support), while racial differences were less pronounced for cumulative stress related to home and work (e.g., negative work-family spillover and higher job demands).

Regarding the variance in physical health outcomes explained by cumulative stress and demographic factors (Fig. 6), cumulative stress accounted for more variance than individual demographic factors. For example, focusing on number of chronic conditions, AUC_G of s-factor scores accounted for the largest portions of unique variance (range of R^2 = [10.30%, 12.86%]). On average, collapsing across age groups, dimensions of stress explained more variance in number of chronic conditions (average R^2 > 11%) than demographic factors (average R^2 < 5%), and approximately 15% of the variance was collectively explained by demographic factors and cumulative stress for each age group.

Shifting focus to predictors of BMI, the percent of variance explained exhibited a roughly "U" shaped pattern across age groups, peaking among adults in their 40s and 50s at baseline, then decreasing for adults in the 60s and 70s, before increasing again for older adults in their 80s. AUC_G of s-factor scores accounted for small to moderate portions of unique variance in BMI (range of R^2 = [0.82%, 5.62%]). The variance in BMI explained by demographic factors differed across age groups. For example, being Black race rather than White race accounted for 2.38% of the variance among adults in their 40s at baseline, while level of education explained the largest portion of variance among adults in their 60s (R^2 = 4.10), and age-related differences explained the largest portion of variance among older adults (R^2 = 3.67).

Regarding predictors of intermediate activities of daily living, demographic factors and dimensions of cumulative stress explained more variance in early adulthood than later adulthood, yet AUC_G of the s-factor emerged as the strongest predictor for each age group (range of R^2 = [6.17%, 17.66%]). Although smaller in magnitude, level of education also contributed to the explained variance in intermediate activities of daily living and consistently across age groups (range of R^2 = [1.66%, 5.52%]). Similar results emerged for basic activities of daily living (Fig. 6). Consistently across age groups, AUC_G of s-factor scores explained the largest portions of variance (range of R^2 = [4.61%, 12.45%]), while demographic factors explained comparatively less variance. However, level of education was the strongest demographic predictor for each age group (range of R^2 = [2.15%, 5.90%]). Moreover, the total explained variance in basic activities of daily living was larger for younger adults compared to older adults.

Unlike physical health outcomes, a different pattern of results emerged for cognitive health outcomes, specifically for executive function and episodic memory. Compared to physical health outcomes, cumulative stress explained less variance in executive function (range of $R^2 = [1.44\%, 5.23\%]$), especially compared to level of education (range of $R^2 = [4.56\%, 13.21\%]$). Similarly, cumulative stress explained only modest portions of variance in episodic memory across age groups (range of $R^2 = [1.17\%, 3.07\%]$), while sex differences accounted for the largest portions of variance (range of $R^2 = [3.58\%, 10.04\%]$).

5. Discussion

The present study compared the relative merits of a novel approach to model the accumulation of stressors over time, compared to traditional composite scores and linear rates of change, to predict physical and cognitive health outcomes. Area under the curve with respect to ground was consistently the strongest predictor of health outcomes, notably compared to a standardized composite score approach that has been widely used in past studies of cumulative stress, irrespective of the health outcome and across different dimensions of stress. Thus, like endogenous, biological markers of stress reactivity, area under the curve for individual trajectories of self-reported stressors shows promise as a data reduction technique to model the accumulation of stressors in longitudinal studies. Crucially, combined with a factor analytic approach to measure the simultaneous exposure to multiple stressors at the cross-section (Mann et al., 2021), the present study forwards and validates an analytic technique to simultaneously model two crucial components of cumulative stress: (1) exposure to the co-occurrence of multiple stressors and (2) repeated exposures to stressors that change over time.

Results of multiple regressions and relative weights analysis suggests that the accumulation of stressors, as indicated by discrimination exposure, home and work-related stress, perceived inequality, stressors related to personal relationships, and financial difficulties, makes unique contributions to the explained variance in physical health outcomes in adulthood, just as much or more so than commonly studied demographic factors, including sex, race/ethnicity, and educational attainment. Conversely, despite cumulative stress significantly predicting executive function and episodic memory, sex differences and educational attainment explained comparatively more variance in these cognitive health outcomes. Results also suggest that the contributions of demographic factors and cumulative stress to the prediction of health outcomes remain stable across adulthood for some outcomes, like the number of chronic conditions, yet wax and wane for other outcomes, like executive function and adiposity indicated by elevated BMI. On the other hand, the prediction of physical functional limitations by demographic factors and cumulative stress is stronger for younger adults than older adults.

The present study also found that levels of cumulative stress were higher at midlife compared to late adulthood. Compared to females, males reported slightly lower levels of cumulative stress, and Black race/ethnicity and other non-White race/ethnicity reported higher levels of cumulative stress than White adults. On the other hand, educational attainment was associated with lower levels of cumulative stress. These findings are consistent with previous studies that have found sex and race/ethnicity differences in cumulative stress (Mann et al., 2021; Sternthal et al., 2011).

The focus of the present study was measuring simultaneous and repeated exposures to multiple psychosocial stressors, which relies on self-report measures and, consequently, are inherently subjective. Future studies will benefit from incorporating objective measures of stressors when modeling cumulative stress. The inherently subjective nature of psychosocial stressors may lead some to worry that the measure of stressors in the present study was confounded by individual differences in personality. However, the overall pattern of results from relative weights analysis was similar after adjusting for the effects of the Big Five domains of personality on health outcomes, and including the individual subordinate dimensions of stress, instead of the general, higher-order, s-factor (Table S6). Whether individual differences in personality mediate or moderate the effects of cumulative stress on health outcomes remain open questions that are beyond the scope of the present study.

5.1. Limitations

We do not claim to have identified a cross-cultural or universal number of dimensions of stress that best correspond to theory, balance model parsimony with explanatory power, or provide an exhaustive or ideal coverage of the relevant content space. On the contrary, the multidimensional structure of stress documented in the present study depended not only on the patterns of correlations among different stressors but also the sample size and the number of stressors that were included in the analysis. If more stressors were measured and included in factor analysis models, then it is entirely possible that many more dimensions of stress would emerge and embed themselves somewhere within, or on the peripheral of the hierarchical model reported in the present study. A cross-cultural, quantitative, lexical approach is needed to determine how many dimensions of cumulative stress exist and whether the number of dimensions change within or across cultures. A lexical hypothesis states: the stressors that are most salient and relevant in people's lives are described by language, so, if a stressor exists, then a word exists to name it (Allport and Odbert, 1936). Exciting developments in machine learning and natural language processing models have the potential to aid in and expedite such efforts soon (Culter et al., 2023).

A key limitation of the present study is reliance on self-reports to measure psychosocial stressors and the absence of objective physical measures of environmental stressors. Another key limitation is the omission of many emotionally salient and physically traumatic stressors that undoubtedly contribute to variation in the health outcomes investigated here, as well as many other mental and physical health outcomes that were not included in the present study; relevant acute and chronic stressors include extreme poverty, loss of personal property, interparental conflict, negative peer influence, bullying, parental psychopathology and drug use, parental incarceration, bereavement, neglect, abuse, harassment, physical and sexual assault, exposure to environmental toxins, noise pollution, crowding, poor quality of housing and schooling, homelessness, social isolation, and exposure to family, community, and mass violence, as well as other traumatic events.

In addition to omitting key stressors, the ages of participants in the present study covered a wide range of midlife and later adulthood, with most participants in their thirties to eighties but, nonetheless, failed to measure stressors during childhood and adolescence. Future studies stand to benefit from measuring a wide swathe of stressors during childhood, through adolescence, and into adulthood using repeated measures in a single study. That way, stress researchers can continue to better understand and empirically document the heterotypic continuity of cumulative stress and the implications for optimizing the measurement of cumulative stress across different life stages to increase the prediction of health outcomes. Thus, the absence of childhood stressors is another key limitation of the present study, and evidence suggests childhood stressors are more salient for some health outcomes than others (Evans et al., 2013b). Future studies stand to benefit from incorporating childhood stressors into models of cumulative stress to further delineate the impact of stress on health.

Whether factor analysis is reliable when repeated across different samples is an empirically open-ended question. In prior work (Mann et al., 2021), however, we have demonstrated that the results of factor analysis models for measures of psychosocial stressors are remarkably stable across different samples, despite substantial differences in economic conditions across those samples. Moreover, a small ($n = 87$) prospective study of Black American children (Burchinal et al., 2000) reported a similar pattern of factor loadings for indicators of social risk across the first four years of life, indicating that results of factor analysis models can be stable across early childhood. Moreover, the present study provides evidence for the longitudinal measurement invariance of the hierarchical model of cumulative stress, indicating that factor loadings remain relatively stable from midlife to later adulthood. Ultimately, the results of factor analysis models are influenced by the sample size, the number of indicators, and the correlations among indicators. If correlations among psychosocial stressors are relatively stable across different samples, then so will the results of factor analysis models (that is, assuming model estimators, factor extraction techniques, and rotation methods for EFA are held constant). Given that prior work has demonstrated that a sample size of $n = 250$ is needed to obtain stable estimates of correlation coefficients (Schönbrodt et al., 2013), we are confident that the present study is sufficiently large to obtain stable estimates. Nevertheless, future studies should assess the generalizability of our findings by testing whether the pattern of factor loadings is similar in other large studies with similar measures.

Although the present study tested longitudinal links between a rich array of stressors and health outcomes, non-linear effects were not examined. Thus, the possibility of curvilinear effects in relation to cumulative stress and health remains an intriguing possibility. For instance, there may be a level of cumulative stress that is so high and unbearable that the consequent effects on health exceed a linear function. Alternatively, there may exist a golden middle (Taylor, 2006) or optimal level of stress, such that both higher and lower levels of stress result in deleterious health. Future studies should consider applying regression models that enable the estimation of curvilinear effects, including polynomial regressions, general additive models, or the two-lines test, as was done recently to test the relevance of the maladaptive poles of major trait domains in relation to well-being (Hobbs et al., 2023).

One strength of the factor analytic techniques that were used to derive the hierarchical model of cumulative stress is the ability to differentiate construct variance from unsystematic measurement error, which increases predictive validity by decreasing nuisance variance that is the result of sampling variability. However, in the present study, we calculated AUC to extend the hierarchical model that was developed at the cross-section to account for repeated exposures to psychosocial stressors over time, which involves the estimation of factor scores, in turn, reintroducing indicator specific error to the measurement of stressors. Consequently, the effects of cumulative stress on health outcomes documented in the present study are likely underestimates of their true population parameters.

The present study also relied on Thomson's regression or exact score method to estimate factor scores (Thomson, 1935; Estabrook et al., 2013), which combines information from the factor loading matrix, the inverse of the observed covariance matrix, and the observed data to specify linear combinations of observed variables to define factor scores (Estabrook et al., 2013). Although this approach is commonly used in applied research, there is a family of related yet alternative methods for estimating factor scores (Grice, 2001; Estabrook et al., 2013), which were not examined in the present study. Evaluating the relative merits of alternative methods for estimating factor scores was beyond the scope of the present study yet remains an interesting direction for future research. Related, the present study provides evidence that total AUC of factor scores outperforms unit-weighted composite scores and a cumulative risk index (i.e., a sum of dichotomized stressors) when predicting health outcomes. However, it is unclear whether the weighting of factor scores, the calculation of total AUC, or both contributed to the increased prediction of health, that is, relative to the composite scores that have historically been used in studies of cumulative stress. Again, future studies stand to benefit from comparing the predictive validity of additional scoring schemes when testing the impact of cumulative stress on health.

The bandwidth-fidelity problem (Cronbach et al., 1957; Cronbach, 1949) has received little to no attention in relation to the measurement of cumulative stress, with at least one noteworthy exception (Sternthal et al., 2011), despite not being framed in such terms. The bandwidth-fidelity problem refers to the concession between the use of constructs or models that cover extensive variance within a particular content space (e.g., the s-factor of cumulative stress), and constructs or models that focus more narrowly on a smaller subset of variables (e.g., subordinate factors of stress and individual stressors). The aim of the present study was not to assess the bandwidth-fidelity trade-off when predicting health outcomes, yet, nevertheless, results shed light on this topic. For instance, AUC_G for s-factor scores, which cover the broadest available content space, outperformed AUC_G for subordinate factor scores, which cover a more narrowly defined content space, *only* for a limited number of health outcomes and subordinate dimensions of stress. AUC_G for s-factor scores was more strongly related to the number of chronic conditions and intermediate activities of daily living than the AUC_G for home and work-related stress, but point estimates were similar for the remaining combinations of stress factors and health outcomes. It remains unknown whether the greater bandwidth provided at the subordinate or high-order level of analysis outperforms the increased fidelity of individual measures of stress when predicting health outcomes. This is yet another important avenue for future studies to navigate.

Finally, there are limitations to the use of AUC to model repeated exposures to stressors. AUC does not distinguish increases from decreases in stressors and, in turn, is not influenced by the direction of change. Put differently, it is possible that two individuals have the same AUC, while stressors increase for one and decrease for the other. Thus, AUC cannot be used to test theories or hypotheses for which the direction of change is pivotal. Of course, this is also true of traditional composite scores, including a standardized continuous score and a cumulative risk index. AUC also doesn't account for the periodicity of change in stressors, as the intervals between waves of data collection are largely determined by recruitment and data collection procedures. Thus, naturally occurring individual differences in the tendency of stressors to recur at shorter or longer intervals of time is not captured by AUC, particularly when AUC is used to capture repeated exposures in a traditional longitudinal study, whether it be a cross-sequential or panel design. It remains unknown whether the predictive strength of AUC will change in studies that measure stressors using ecological momentary assessment, which would better allow for naturally occurring variability in the periodicity of stressors.

5.2. Implications

In conclusion, the present study provides needed construct validation efforts (Cronbach et al., 1955) by examining the most appropriate model and data reduction technique to operationalize the accumulation of stressors. Results indicate that a higher-order factor model at the cross-section provides an adequate means to operationalize the simultaneous exposure to multiple stressors, while total AUC provided the best model of repeated and cumulative exposures to stressors. Indeed, the prediction of health outcomes increased, on average, by over 120% when the accumulation of stressors was modeled using total AUC of weighted factor scores, compared to traditional unit-weighted composite scores that are commonly used in studies of cumulative stress. In fact, for certain outcomes and dimensions of cumulative stress, there was more than a 10-fold increase in the size of the multiple regression coefficient. Moreover, cumulative stress was anywhere from 2-to-5-fold more predictive of physical health outcomes than any given demographic factor. We encourage others to continue the long, hard, work of improving construct validity to further our understanding of how stressors accumulate to impact physical and cognitive health over the life course.

CRediT authorship contribution statement

Frank D. Mann: Conceptualization, Data curation, Formal analysis, Project administration, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Adolfo G. Cuevas:** Writing – original draft, Writing – review & editing. **Sean A.P. Clouston:** Resources, Supervision, Writing – review & editing. **Colin D. Freilich:** Writing – review & editing. **Zlatan Krizan:** Writing – review & editing. **Sascha Zuber:** Writing – review & editing. **Linda Wänström:** Writing – review & editing. **Graciela Muniz-Terrera:** Writing – review & editing. **Patrick O'Keefe:** Writing – review & editing. **Stacey Voll:** Writing – review & editing. **Scott Hofer:** Writing – review & editing. **Joseph L. Rodgers:** Writing – review & editing. **Robert F. Krueger:** Supervision, Writing – review & editing.

Data availability

Data from the MIDUS study is publically available online to all interested investigators.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.socscimed.2024.116787.

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