Stressful life events across the lifespan and inflammation: an integrative data analysis of the HRS and ELSA cohorts

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STRESS MEASUREMENT NETWORK

Accumulation of risks model

- **Total number** of stressful life events has a cumulative effect on physiological health. Supported by nationally representative cohort studies

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  - Health and Retirement Study: **CRP** (Elliot et al., 2017: specifically found effects at low levels of perceived control)

Sensitive period model

- Stressful events during **critical developmental stages** may have more of an influence on physiology.

Sensitive period model

- Stressful events during critical developmental stages may have more of an influence on physiology. Less research comparing life stages:
  - *Both adverse childhood experiences (age 0-15) and adulthood stressors (age 21-44):* higher levels of **suPAR** but not CRP/IL6 (Bourassa et al., 2021)

Specific aims

Aim 1: to test the effect of cumulative stressful life events (total number across the lifespan) on inflammation.

Aim 2: to test the effect of number of stressful events reported during different life stages on inflammation.

Methods

	HRS	ELSA
N participants	5136	2816
Age (mean)	70.6	66.1
Sex (% male)	40.3%	45.8%
BMI (mean)	28.9	28.0
Smoking (% yes)	10.1%	11.9%

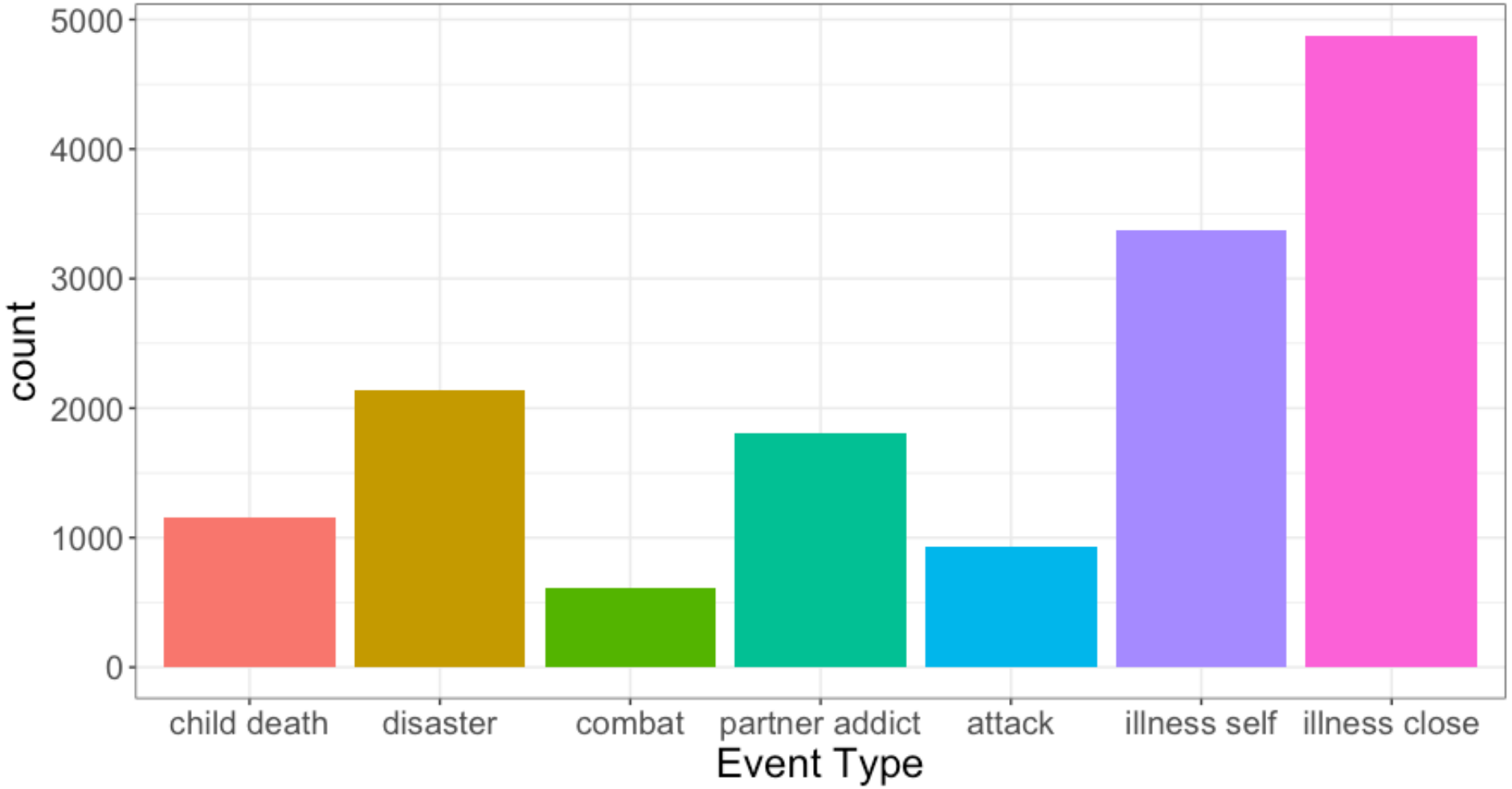
Predictor

Assessment of Stressful Life Events

- 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?
- Did a relative or close friend of yours ever have a life-threatening illness or accident?

Predictor

Methods



Predictor

Assessment of Stressful Life Events

- If participants endorsed any of the 7 events, they provided the year the event took place

PPT 000
Has a child of yours ever died? Yes No
Indicate the age you were when it happened most recently

_____

Predictor

Assessment of Stressful Life Events

- If participants endorsed any of the 7 events, they provided the year the event took place

PPT 000

Has a child of yours ever died? Yes No

Indicate the age you were when it happened most recently

Age 35

_____

Predictor

Life stage ranges for categorizing events

Childhood: 0-17 years

Young Adulthood: 18-39 years

Midlife: 40-59 years

Late adulthood: 60+

Scott et al., 2019; Stebbins et al., 2023; Papilia *Adult development and aging* 2007

Predictor

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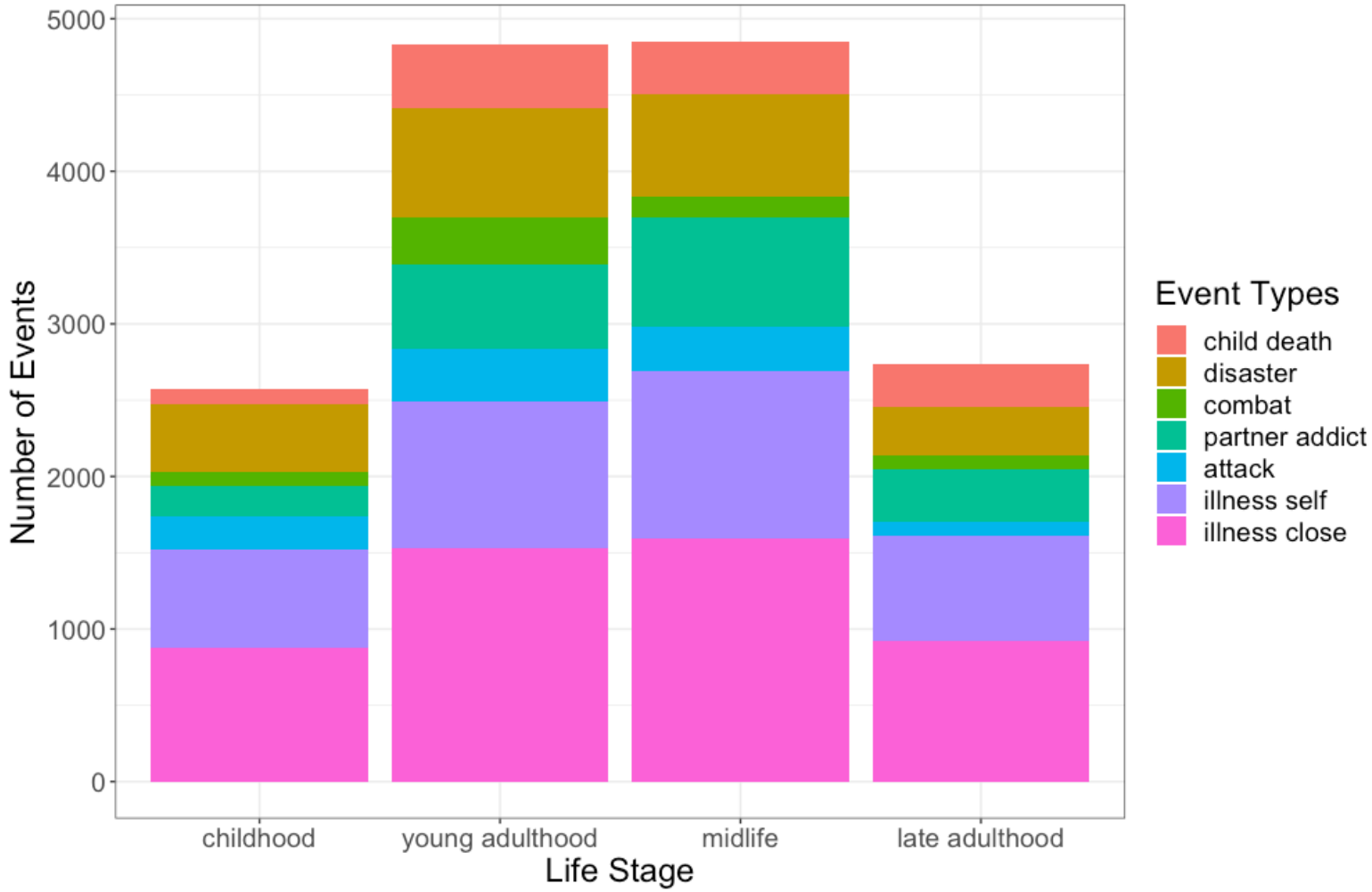
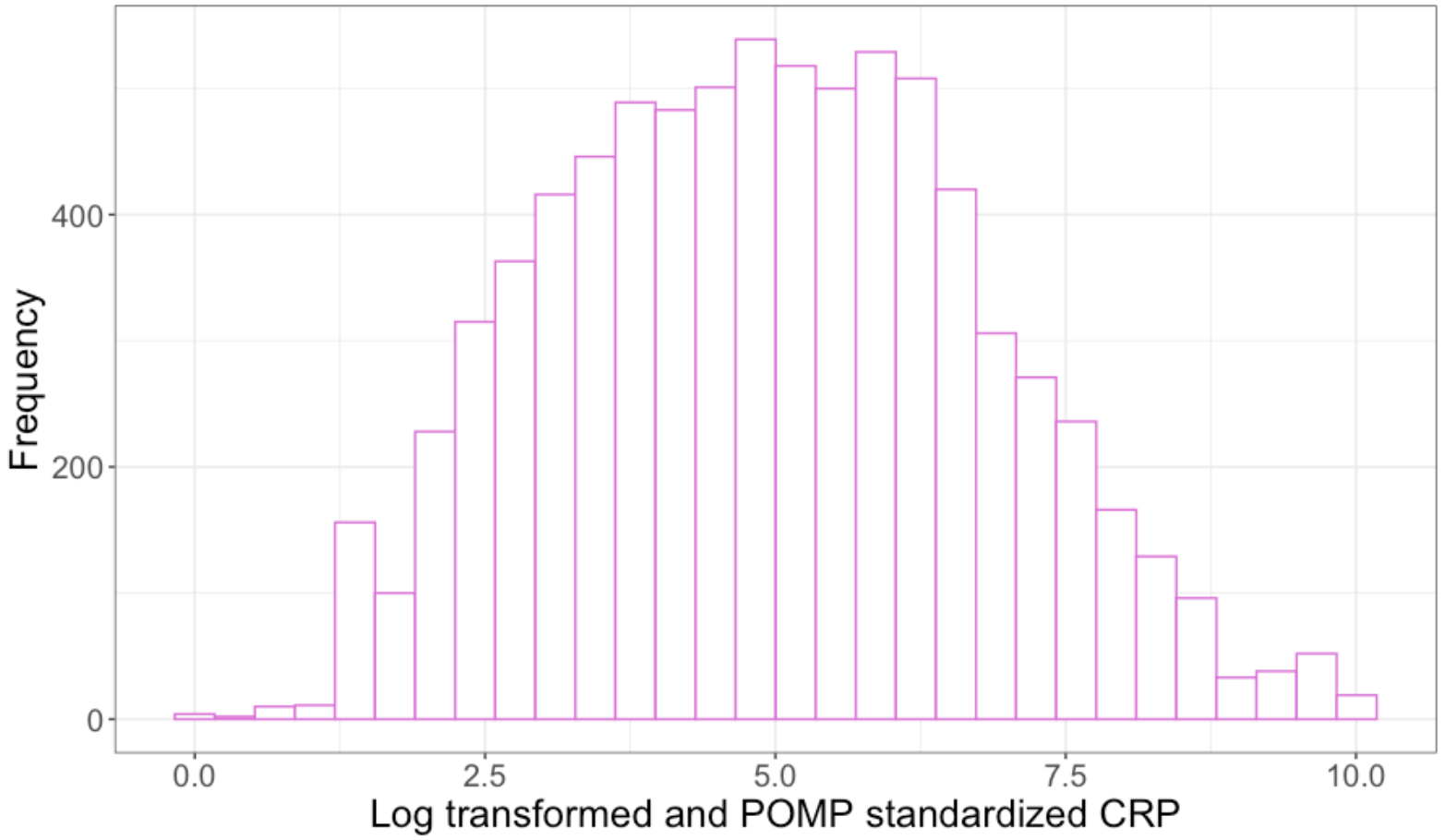


Outcome

Methods

C-reactive protein (mg/L)

1. Excluded outliers (± 3SD)
2. Natural-log transformed
3. Harmonized methodological differences using the Proportion of Maximum Possible (POMP) scores



Lam et al., 2020; Stawaski et al., 2019

Covariates

Primary covariates

- Age
- Sex
- BMI
- Smoking Status (Yes/No)
- Time lapsed between survey and blood draw
- Cohort (ELSA/HRS)

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Primary covariates

- Age
- Sex
- BMI
- Smoking Status (Yes/No)
- Time lapsed between survey and blood draw (*average 5 years; range 2-11 years*)
- Cohort (ELSA/HRS)

Secondary covariates

- Race (white/non-white)
- Education (harmonized 0-14+ years)

Clouston et al., 2020

Model building approach

Analytic Plan

Various stages of model building

Primary analyses

- Cumulative effect
- Lifespan main effects models
- All lifespan stages in the same model

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Sensitivity

- Race education covariates added
- Health related stressor removed from event count
- Drop people CRP >10
- Added childhood specific stressors to event count

Martikainen & Valkonen, 1998; Phillips et al., 2008; Pearson et al., 2003

Results & sensitivity analyses

		Full Sample (N=7,952)	**Race and Education adjusted** (N=7,876)	**Drop Health Stressor** (N= 7,096)	**CRP <= 10** (N=7,389)	**Childhood stressors added** (N=7,925)
Cumulative effect						
Main effects						
Age 0-17	Childhood					
Age 18-39	Young Adulthood					
Age 40-59	Midlife					
Age 60+	Late adulthood					
Independent effects						
	Childhood					
	Young Adulthood					
	Midlife					
	Late adulthood					

Cumulative model

Main effect of total number of stressors on CRP in full sample

	CRP		
Predictors	*Estimates*	*std. Error*	*p*
Intercept	0.07	0.20	0.732
Event Total	**0.05**	**0.02**	**0.012**
Age	**0.02**	**0.00**	**<0.001**
Sex	**0.29**	**0.04**	**<0.001**
BMI	**0.12**	**0.00**	**<0.001**
Smoking	**0.59**	**0.06**	**<0.001**
Time interval	-0.01	0.01	0.243
Cohort	**0.43**	**0.05**	**<0.001**
Observations	**N= 7952**		
Marginal R^2 / Conditional R^2	0.148 / 0.161		

Sex (women)
Smoking (yes)
Cohort (ELSA)

Results & sensitivity analyses

Results

(N~7,952)		Full Sample	Race and Education adjusted	Drop Health Stressor	CRP <= 10	Childhood stressors added
Cumulative effect		p=.012	p=.015	p<.001	p=.052	p=.012

= p < .05

= p < .1

Results & sensitivity analyses

Results

(N~7,952)		Full Sample	Race and Education adjusted	Drop Health Stressor	CRP <= 10	Childhood stressors added
Cumulative effect		p=.012	p=.015	p<.001	p=.052	p=.012
Main effects						
Age 0-17	Childhood					
Age 18-39	Young Adulthood					
Age 40-59	Midlife					
Age 60+	Late Adulthood					

Lifespan main effects

Results

Full Sample

	Childhood			Young Adulthood			Midlife			Late Adulthood		
Predictors	*Estimate*	*std. Error*	*p*	*Estimate*	*std. Error*	*p*	*Estimate*	*std. Error*	*p*	*Estimate*	*std. Error*	*p*
(Intercept)	0.13	0.20	0.495	0.07	0.20	0.722	0.09	0.20	0.648	0.10	0.20	0.602
Childhood	0.01	0.04	0.746									
Young Adulthood				0.06	0.03	**0.037**						
Midlife							0.04	0.03	0.138			
Late Adulthood										-0.03	0.04	0.468
Observations	**N= 7952**			**N= 7952**			**N= 7952**			**N= 7952**		
Marginal R^2 / Conditional R^2	0.148 / 0.162			0.148 / 0.162			0.148 / 0.162			0.148 / 0.162		

Results & sensitivity analyses

Results

(N~7,952)		Full Sample	Race and Education adjusted	Drop Health Stressor	CRP <= 10	Childhood stressors added
Cumulative effect		p=.012	p=.015	p<.001	p=.052	p=.012
Main effects						
Age 0-17	Childhood					
Age 18-39	Young Adulthood	p=.037	p=.042	p=.008	p=.003	p=.042
Age 40-59	Midlife					
Age 60+	Late Adulthood			p=.043		

Results & sensitivity analyses

(N~7,952)		Full Sample	Race and Education adjusted	Drop Health Stressor	CRP <= 10	Childhood stressors added
Cumulative effect		p=.012	p=.015	p<.001	p=.052	p=.012
Main effects						
Age 0-17	Childhood					
Age 18-39	Young Adulthood	p=.037	p=.042	p=.008	p=.003	p=.042
Age 40-59	Midlife					
Age 60+	Late Adulthood			p=.043		
Independent effects (age 65+: N=4,972)						
	Childhood					
	Young Adulthood					
	Midlife					
	Late Adulthood					

Lifespan comparison models

Results

	Sample 65+		
Predictors	*Estimates*	*std. Error*	*p*
Intercept	0.07	0.34	0.840
Childhood	0.01	0.06	0.807
Young Adulthood	0.06	0.04	0.086
Midlife	0.08	0.04	**0.038**
Late Adulthood	0.01	0.04	0.829
Age	0.02	0.00	**<0.001**
Sex	0.22	0.05	**<0.001**
BMI	0.10	0.00	**<0.001**
Smoking	0.63	0.09	**<0.001**
Time interval	-0.01	0.01	0.244
Cohort	0.54	0.07	**<0.001**
Observations	**N= 4972**		
Marginal R^2 / Conditional R^2	0.116 / 0.159		

Results & sensitivity analyses

(N~7,952)		Full Sample	Race and Education adjusted	Drop Health Stressor	CRP <= 10	Childhood stressors added
Cumulative effect		p=.012	p=.015	p<.001	p=.052	p=.012
Main effects						
Age 0-17	Childhood					
Age 18-39	Young Adulthood	p=.037	p=.042	p=.008	p=.003	p=.042
Age 40-59	Midlife					
Age 60+	Late Adulthood			p=.043		
Independent effects (age 65+: N=4,972)						
	Childhood					
	Young Adulthood	p=.086	p=.083	p=.013	p=.028	p=.087
	Midlife	p=.038	p=.038	p=.022	p=.041	p=.039
	Late Adulthood					

Summary

The association with cumulative total and stressors in young adulthood and midlife were consistent in a sample size of almost **8,000 individuals** residing in the US and UK.

They were also largely robust to sensitivity analyses:

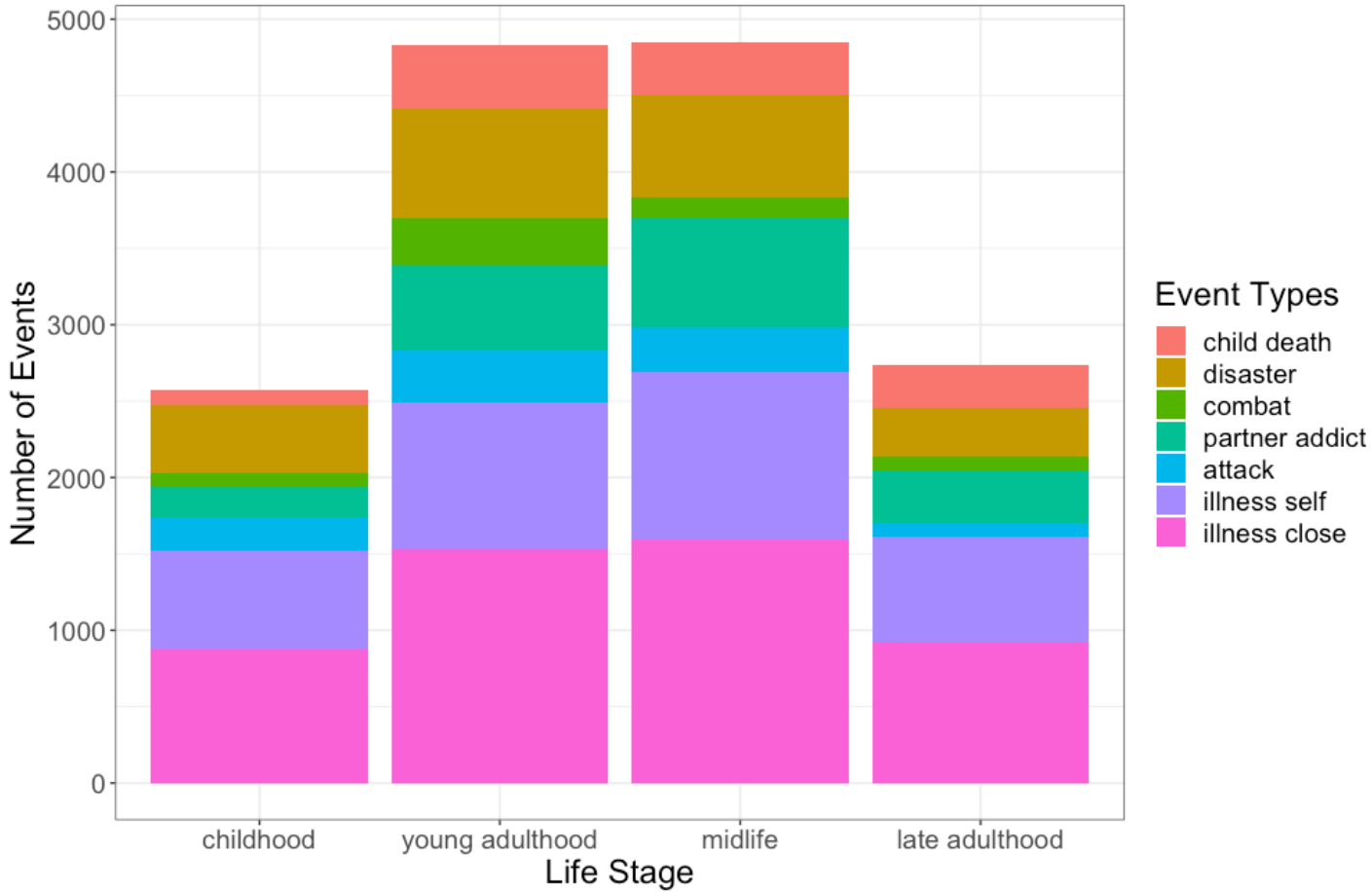
- Controlling for education and race
- Removing individual health related stressors
- Removing individuals who may have acute illness (CRP>10)
- The addition of childhood specific stressors

Why young adulthood & midlife?

Discussion and Future Directions

Individuals in these life stages may not only experience these stressors but also hold the most responsibility as (emotional and tangible) support providers in stressful situations.

E.g., caregiving



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