RCCN Workshop
Life Course Perspectives on Aging

Designs for Life Course Studies

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November 4, 2020

RESEARCH CENTERS
COLLABORATIVE NETWORK
of the National Institute on Aging, NIH

Agenda

I. **Review: Study designs for life course studies**

II. Boston Early Adversity & Mortality Study (BEAMS)

III. Challenges and research opportunities in early adversity and lifespan health

Life Course Epidemiological Study Designs

Observational designs

- Prospective cohort studies
- Case-control studies
- Cross-sectional studies

Quasi- or Natural experimental designs

Experimental designs

Observational Designs (I)

Key features:

- Observe & record info on exposure & outcomes
- No manipulation

Benefit vs. Limitation:

\+ Minimum ethical issues

\- Weaker causal inference

Prospective cohorts

- Strong evidence for temporality of IV-DV relationship
- Key concerns: Sample representativeness; drop-out & loss to follow-up
- Variations
  - Birth (& perinatal) cohorts; high-risk cohorts; twin cohorts

Observational Designs (II)

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- Variations
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Case-control studies

- Participants selected *after* outcome has been ascertained
- (+) Cost-effectiveness vs. (-) Recall bias & selection bias

Observational Designs (III)

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Prospective cohorts

- Strong evidence for temporality of IV-DV relationship
- Key concerns: Sample representativeness; drop-out & loss to follow-up
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Case-control studies

- Participants selected *after* outcome has been ascertained
- (+) Cost-effectiveness vs. (-) Recall bias & selection bias

Cross-sectional studies

- Informs prevalence & initial clues re: potential associations, but weak design for causality
- Convenience or representative samples

Quasi- / Natural Experimental Designs

Key features

- "Assignment" into exposed vs. unexposed group via an event (e.g., educational reform, Dutch famine)

Benefit vs. Limitation

\+ Less subject to selection bias

\- Information bias
\- Non-random assignment of exposure
→ Confounding

Experimental Designs

Key features

- Random assignment
  - Assumption: Groups are interchangeable except for exposure (treatment) status
- Researchers manipulate exposure

Benefit vs. Limitation

+ Gold standard for causal inference
+ No selection bias

- Practical and ethical concerns

Agenda

I. Review: Study designs for life course studies

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Adverse Childhood Experiences (ACEs)

Research Article

Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults

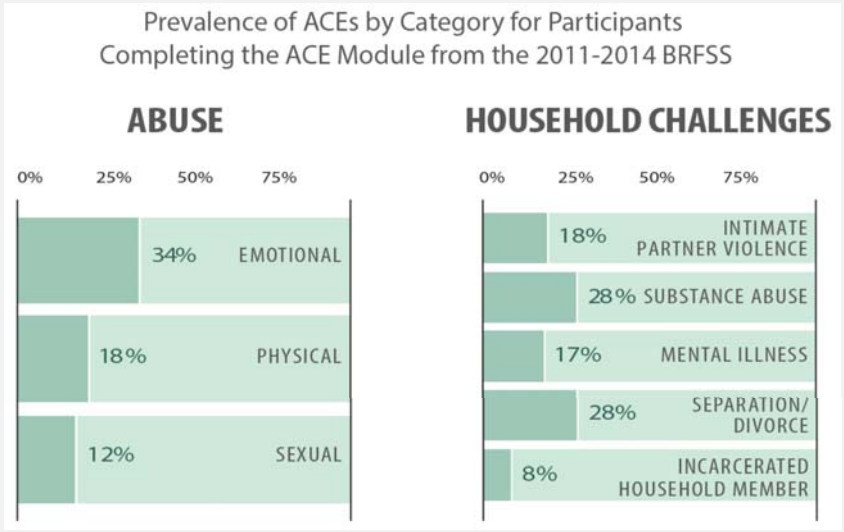
The Adverse Childhood Experiences (ACE) Study

Vincent J. Felitti, MD, FACP, Robert F. Anda, MD, MS, Dale Nordenberg, MD, David F. Williamson, MS, PhD, Alison M. Spitz, MS, MPH, Valerie Edwards, BA, Mary P. Koss, PhD, James S. Marks, MD, MPH

Background: The relationship of health risk behavior and disease in adulthood to the breadth of exposure to childhood emotional, physical, or sexual abuse, and household dysfunction during childhood has not previously been described.

Methods: A questionnaire about adverse childhood experiences was mailed to 13,494 adults who had completed a standardized medical evaluation at a large HMO; 9,508 (70.5%) responded. Seven categories of adverse childhood experiences were studied: psychological, physical, or sexual abuse; violence against mother; or living with household members who were substance abusers, mentally ill or suicidal, or ever imprisoned. The number of categories of these adverse childhood experiences was then compared to measures of adult risk behavior, health status, and disease. Logistic regression was used to adjust for effects of demographic factors on the association between the cumulative number of categories of childhood exposures (range: 0–7) and risk factors for the leading causes of death in adult life.

Results: More than half of respondents reported at least one, and one-fourth reported ≥2 categories of childhood exposures. We found a graded relationship between the number of categories of childhood exposure and each of the adult health risk behaviors and diseases that were studied ($P < .001$). Persons who had experienced four or more categories of childhood exposure, compared to those who had experienced none, had 4- to 12-fold increased health risks for alcoholism, drug abuse, depression, and suicide attempt; a 2- to 4-fold increase in smoking, poor self-rated health, ≥50 sexual intercourse partners, and sexually transmitted disease; and a 1.4- to 1.6-fold increase in physical inactivity and severe obesity. The number of categories of adverse childhood exposures showed a graded relationship to the presence of adult diseases including ischemic heart disease, cancer, chronic lung disease, skeletal fractures, and liver disease. The seven



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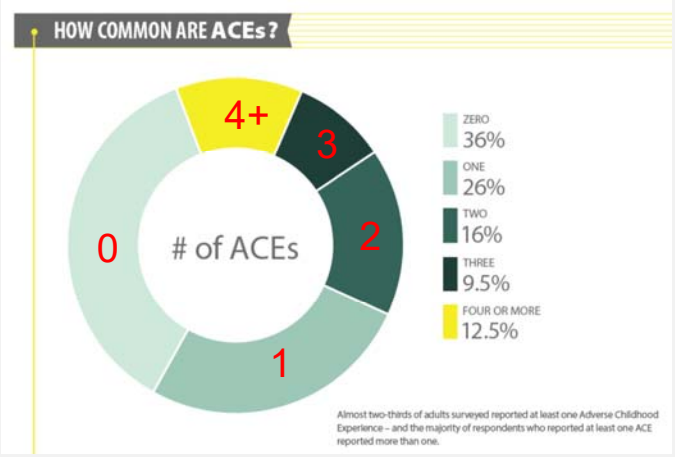

Felitti et al. (1988) *Am J Prev Med*; Merrick et al. (2018), *JAMA Pediatr*; https://vetoviolence.cdc.gov/apps/phl/resource_center_infographic.html

ACEs and Adulthood Health

Pooled ORs (95%CI) for 4+ vs. 0 ACEs	
Suicide attempt	30.1 (14.7–61.7)
Problem drug use	10.2 (7.6–13.7)
STDs	5.9 (3.2–10.9)
Problem drinking	5.8 (4.0–8.6)
Depression	4.4 (3.5–5.5)
Early sexual initiation	4.2 (3.0–5.9)
Teenage pregnancy	3.7 (2.9–4.8)
Respiratory disease	3.1 (2.5–3.8)
Liver / Digestive dis.	2.8 (2.3–3.4)
Cancer	2.3 (1.8–3.0)
CVD	2.1 (1.7–2.6)
Diabetes	1.5 (1.2–1.9)
Obesity / Overweight	1.4 (1.1–1.7)
Physical inactivity	1.3 (1.0–1.5)

Hughes et al. (2017) *Lancet Public Health*

Sample & F/U	ACEs measure	Key Findings
[1]CDC-Kaiser ACE Study *N* = 17,337 1995-2006	#ACEs categories (0-8); retrospective	**6+ vs. 0 ACEs: HR=1.7** **deaths ≤ age 75 only** Very weak assoc. btw fewer ACESs categories & premature death.
[2]UK 1958 Birth Cohort Study *N* = 15,221 1958-2008	# ACEs categories (0-6); Qs to teacher & parents asked in childhood	**Men: Threshold effect** 2+ vs. 0 ACEs: HR = 1.6 **Women: Gradient effect** 2+ vs. 0 ACEs: HR = 1.8 1 vs. 0 ACEs: HR = 1.7
[3]MIDUS *N* = 6,285 1995-2015	Abuse types (0-2), retrospective: - Emotional - Moderate physical - Severe physical	**Men: No association** **Women: Gradient effect** 3 vs. 0: HR = 1.7 1-2 vs. 0: HR = 1.2

[1]Brown et al. (2009) *Am J Prev Med*; [2]Kelly-Irving et al. (2013) *Eur J Epidemiol*; [3]Chen et al. (2016) *JAMA Psychiatry*

Barriers to Scientific Progress: Early Adversity & Lifespan Health

- Focus on one / single category of stressors
  - ACEs
  - Childhood SES
  - Environmental hazards: built environment, pollution
  - One-time event: famine, extreme cold, economic downturn
- However, early risk factors tend to co-occur
- Limited understanding of mechanistic pathways
  - Exposure dimensions → Outcome?
  - Intersection with developmental timing
  - Inadequate longitudinal “lifespan” data
- Measurement issues
  - Retrospective report
  - Focus on severe experiences
  - Assumptions re: operationalization (cumulative score, any vs. none, etc.)

Barriers to Scientific Progress: Early Adversity & Lifespan Health

Table 1 Stressor Exposure for Each Domain of Multiple Stressors

Evans & English (2002), *Child Dev*

	Poverty		Middle Income			
Stressor Domain	*M* (*SD*)	% Exposed	*M* (*SD*)	% Exposed	*t* test	χ^2 test
Density	.68 (.21)	16	.50 (.13)	7	8.15**	4.60*
Noise	64.98 (6.84)	32	61.30 (7.29)	21	3.97**	4.53*
Housing problems	.74 (.30)	24	.42 (.22)	3	9.96**	25.70**
Family turmoil	2.25 (1.42)	45	1.05 (1.11)	12	7.13**	35.20**
Family separate	2.56 (1.34)	45	1.26 (1.16)	14	7.82**	30.47**
Violence	.22 (.24)	73	.10 (.19)	49	3.67**	16.99**

Note: Percentage exposed = >1 *SD* above the mean, except for violence wherein any exposure was counted. Mean (*SD*) = actual exposure levels.
*$p < .05$; **$p < .01$.

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- Exposure dimensions
- Intersection with deve
- Inadequate longitudin

o Measurement issues
- Retrospective report
- Focus on severe expe
- Assumptions re: operationalization (cumulative score, any vs. none, etc.)

Table 2. Multiple risk exposure and parental education

Evans & Kim (2010), *Ann NY Acad Sci*

	Parental educational level		
Measure of proximal environmental experiences	No high school	High school	College
Family intellectual/cultural climate	4.21	4.58	5.42
Family active-recreational climate	4.90	5.36	5.97
Mother rejection	4.13	3.46	2.94
Family social support	14.73	15.26	16.59
Belonging at school	2.19	2.41	2.64
Negative life events	4.74	3.63	3.27
Daily hassles	151.76	139.00	138.67

Barriers to Scientific Progress: Early Adversity & Lifespan Health

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  - ACEs
  - Childhood SES
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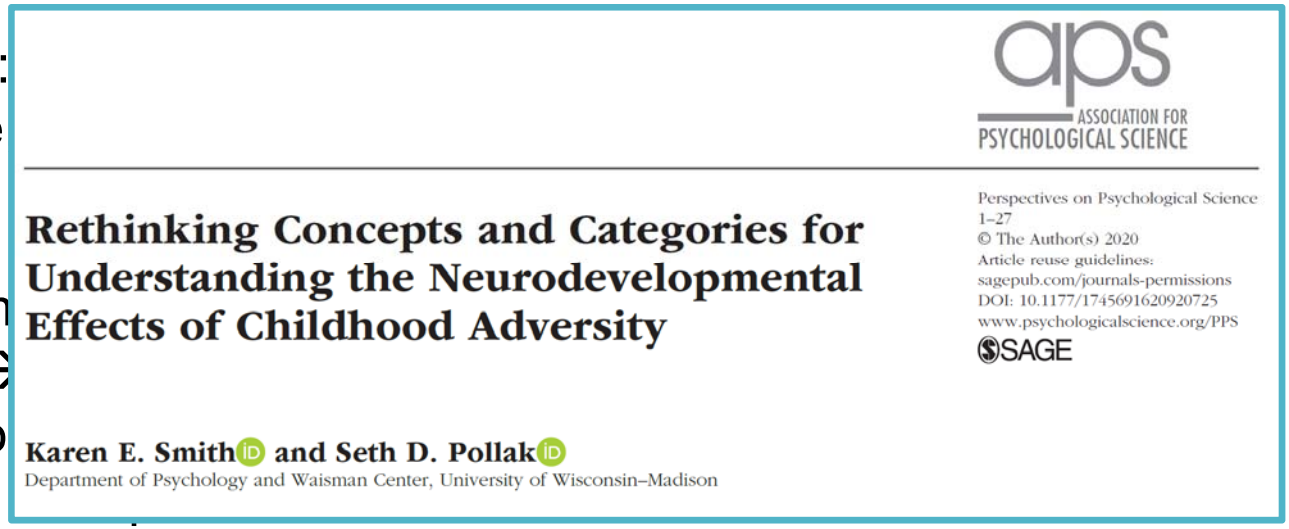


aps ASSOCIATION FOR PSYCHOLOGICAL SCIENCE

Rethinking Concepts and Categories for Understanding the Neurodevelopmental Effects of Childhood Adversity

Karen E. Smith and Seth D. Pollak
Department of Psychology and Waisman Center, University of Wisconsin–Madison

Perspectives on Psychological Science
1–27

DOI: 10.1177/1745691620920725
www.psychologicalscience.org/PPS
SAGE

Boston Early Adversity & Mortality Study (BEAMS)

Primary objectives:

1. Create a birth-to-death dataset using 3 long-running studies of aging
   - o Administrative data linkage to acquire prospective data on:
     - Early-life socioeconomic & environmental conditions via administrative record linkage
     - Later-life health
   - o Extend linkage to siblings
2. Examine prospecctive associations from early adversity dimensions to later-life health outcomes, and evaluate long-term explanatory pathways

BEAMS Cohorts (overall N = 3004)

	Normative Aging Study (NAS), N = 2280	Glueck Study N = 456	Grant Study N = 268

Sample	• Community-dwelling men in greater Boston
	• Inclusion:
	  • Absence of major diseases
	  • Geographic stability
		• Boston public school boys -- matched controls (on age, ethnicity, IQ, neighborhood criminality) for a prospective study on juvenile delinquency	• Harvard sophomores recruited for an intensive multidisciplinary study of psychological health
			• Free of emotional, physical, & academic difficulties

Year enrolled	1961-70	1938	1938
Age at enrollment, M (SD)	42 (9)	14 (2)	19 (2)
Birth year, M (SD)	1924 (9)	1929 (2)	1920 (2)
% deceased	74% (Aug 2018)	80% (Aug 2019)	96% (Jan 2019)

BEAMS Administrative Record Linkage

I. Pre-linkage

- Code identifiers & ancillary data for participants (P) & siblings (S):
  - Full name
  - Date of birth
  - Residential history
  - Parental information (name, age, origin)

II. "Hand-linkage" to Ancestry & FamilySearch

- Using data from Step 1, link each P & S to:
  - 1900-1940 US Census
  - State/town birth records
  - State death records, SSDI
  - Military/Veteran records (draft cards, enlistment records, BIRLS)
  - Social Security Application & Claims Index
  - Misc: e.g., obituaries
- **Key information:**
  - **Family-of-origin & neighborhood SES**
  - **Family composition**
  - Unreported sibs
  - Add'l identifiers to facilitate further linkage (e.g., SSN, mortality info)

III. Additional linkages

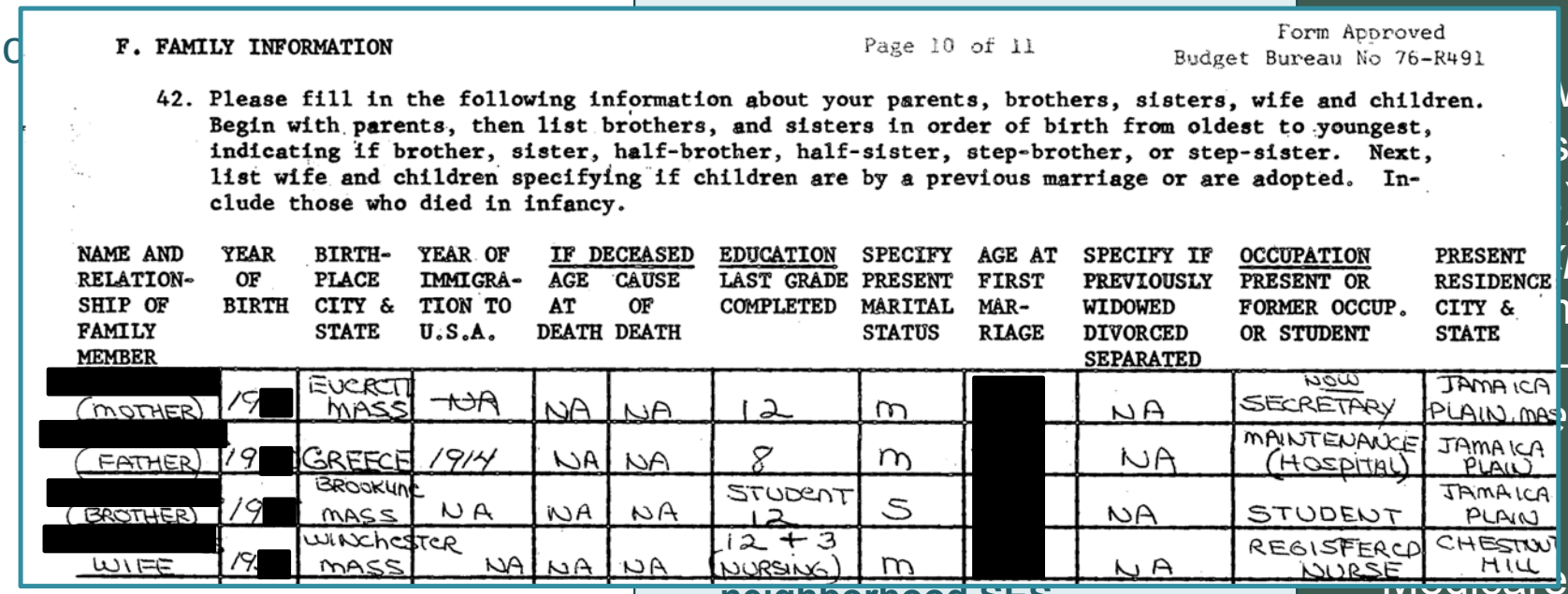
- **Early-life lead exposure:**
  - Boston Water & Sewer Commission (and similar agencies) – *water pipe-based exposure*
  - Environmental Protection Agency – *airborne exposure*
- **Later-life health outcomes**
  - Medicare records
  - National Death Index

BEAMS Administrative Record Linkage

I. Pre-linkage

II. "Hand-linkage" to Ancestry & FamilySearch

III. Additional linkages



F. FAMILY INFORMATION — Page 10 of 11 — Form Approved Budget Bureau No 76-R491

42. Please fill in the following information about your parents, brothers, sisters, wife and children. Begin with parents, then list brothers, and sisters in order of birth from oldest to youngest, indicating if brother, sister, half-brother, half-sister, step-brother, or step-sister. Next, list wife and children specifying if children are by a previous marriage or are adopted. Include those who died in infancy.

NAME AND RELATIONSHIP OF FAMILY MEMBER	YEAR OF BIRTH	BIRTHPLACE CITY & STATE	YEAR OF IMMIGRATION TO U.S.A.	IF DECEASED AGE AT DEATH	IF DECEASED CAUSE OF DEATH	EDUCATION LAST GRADE COMPLETED	SPECIFY PRESENT MARITAL STATUS	AGE AT FIRST MARRIAGE	SPECIFY IF PREVIOUSLY WIDOWED DIVORCED SEPARATED	OCCUPATION PRESENT OR FORMER OCCUP. OR STUDENT	PRESENT RESIDENCE CITY & STATE
[redacted] (MOTHER)	19[redacted]	EUCRCTI MASS	NA	NA	NA	12	m	[redacted]	NA	NOW SECRETARY	JAMAICA PLAIN, MASS
[redacted] (FATHER)	19[redacted]	GREECE	1914	NA	NA	8	m		NA	MAINTENANCE (HOSPITAL)	JAMAICA PLAIN
[redacted] (BROTHER)	19[redacted]	BROOKLINE MASS	NA	NA	NA	STUDENT 12	S		NA	STUDENT	JAMAICA PLAIN
[redacted] WIFE	19[redacted]	WINCHESTER MASS	NA	NA	NA	12 + 3 (NURSING)	m		NA	REGISTERED NURSE	CHESTNUT HILL

neighborhood SES

- **Family composition**
- Unreported sibs
- Add'l identifiers to facilitate further linkage (e.g., SSN, mortality info)

lead exposure:

Water & Sewer

sion (and similar

) – *water pipe-*

posure

nental Protection

- airborne

health outcomes

records

- National Death Index

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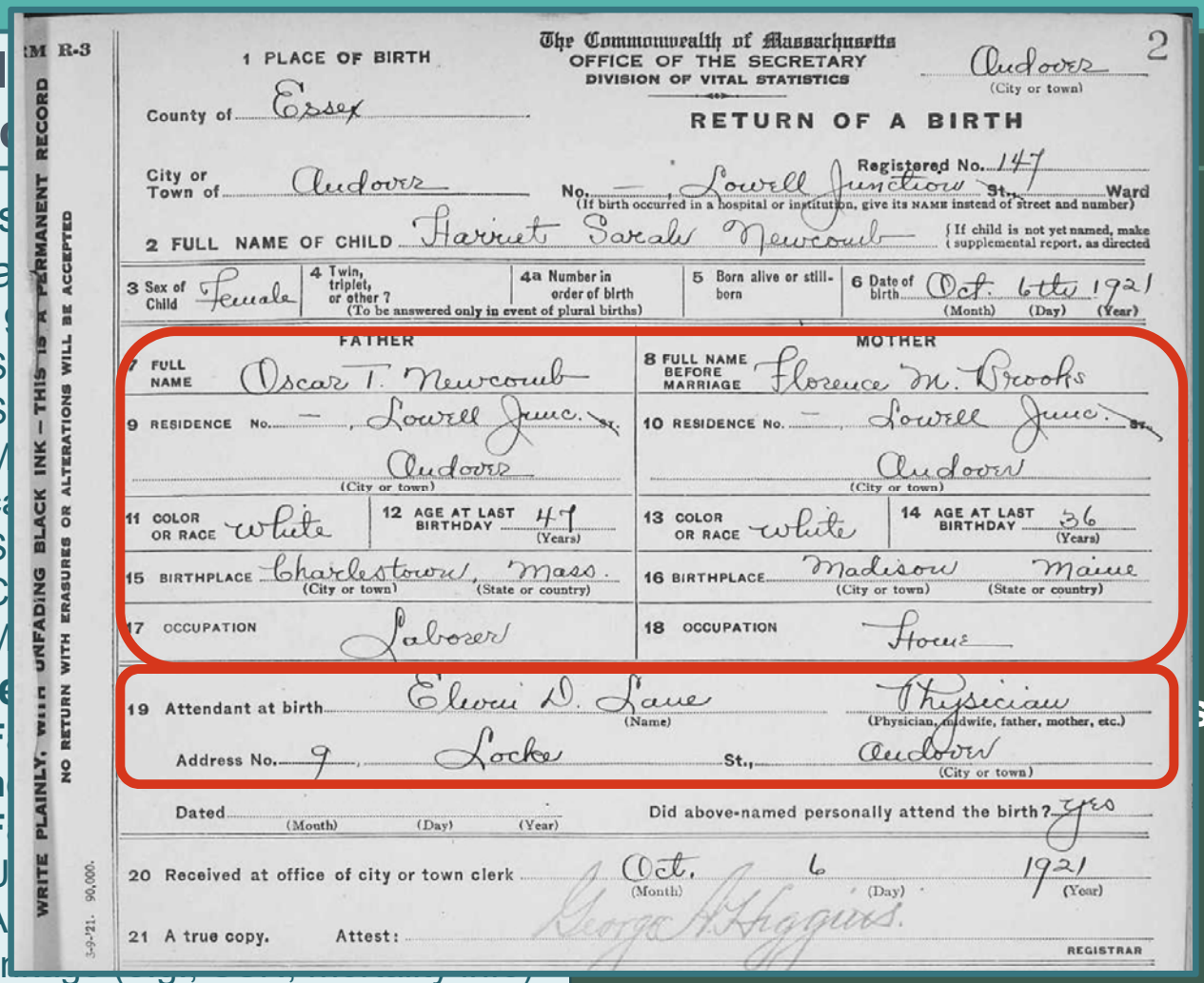


M R-3

WRITE PLAINLY, with UNFADING BLACK INK — THIS IS A PERMANENT RECORD
NO RETURN WITH ERASURES OR ALTERATIONS WILL BE ACCEPTED

The Commonwealth of Massachusetts
OFFICE OF THE SECRETARY
DIVISION OF VITAL STATISTICS

RETURN OF A BIRTH

2

1 PLACE OF BIRTH
County of Essex
City or Town of Andover (Andover (City or town))
Registered No. 147
No. — Lowell Junction St., Ward
(If birth occurred in a hospital or institution, give its NAME instead of street and number)

2 FULL NAME OF CHILD Harriet Sarah Newcomb
{If child is not yet named, make supplemental report, as directed

3 Sex of Child	4 Twin, triplet, or other ? (To be answered only in event of plural births)	4a Number in order of birth	5 Born alive or still-born	6 Date of birth
Female				Oct. 6th 1921 (Month) (Day) (Year)

FATHER	MOTHER
7 FULL NAME: Oscar T. Newcomb	8 FULL NAME BEFORE MARRIAGE: Florence M. Brooks
9 RESIDENCE No. — Lowell Junc. St. Andover (City or town)	10 RESIDENCE No. — Lowell Junc. St. Andover (City or town)
11 COLOR OR RACE: White; 12 AGE AT LAST BIRTHDAY: 47 (Years)	13 COLOR OR RACE: White; 14 AGE AT LAST BIRTHDAY: 36 (Years)
15 BIRTHPLACE: Charlestown (City or town), Mass. (State or country)	16 BIRTHPLACE: Madison (City or town), Maine (State or country)
17 OCCUPATION: Laborer	18 OCCUPATION: Home

19 Attendant at birth: Elwin D. Lane (Name); Physician (Physician, midwife, father, mother, etc.)
Address No. 9 Locke St., Andover (City or town)

Dated (Month) (Day) (Year)
Did above-named personally attend the birth? Yes

20 Received at office of city or town clerk: Oct. (Month) 6 (Day) 1921 (Year)

21 A true copy. Attest: George A. Higgins REGISTRAR

3-9-21. 90,000.

BEAMS Administrative Record Linkage

GSA narrated poster:

Program Area: Behavioral and Social Sciences

Category: Poster

Session: Social Determinants of Health

(2953) Applying Administrative Linkage to Longitudinal Aging Studies: Boston Early Adversity and Mortality Study

(2953-A) Social Determinants of Health 1: Presenter Discussion
Wednesday, November 4, 2020
1:45 PM – 2:15 PM

Preliminary Data - BEAMS Administrative Record Linkage

Findings from Ancestry & FamilySearch linkage completed to date:

	NAS *N = 2280	Glueck *N = 456	Grant *N = 268
Longitudinal cohort participants			
N (% of cohort)	1260 (55%)	117 (26%)	251 (94%)
% matched to 1+ Census	93%	88%	94%
Avg. number of siblings	3.4	3.6	2.2
Siblings			
N	4334	423	561
% female	51%	45%	48%
% matched to 1+ Census	84%	87%	92%
Year of birth, range	1878 - 1964	1903 - 1946	1904 - 1934

* denotes sample size of the original cohort.

Total number of participants and siblings with completed Ancestry & FamilySearch linkage (Nov 2020):
6946 (56% of all families)

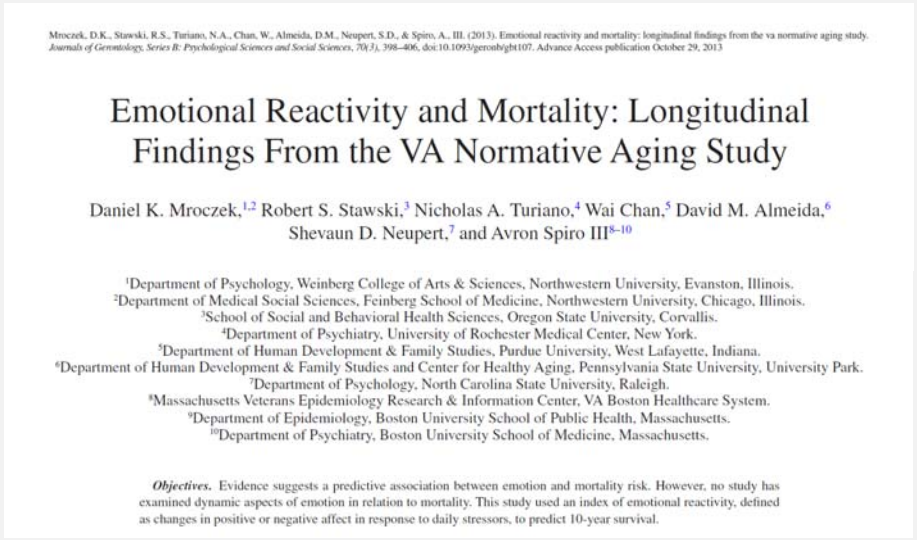
BEAMS Scientific Questions

1. Do early adversities in the socioeconomic, environmental, and psychosocial domains have unique & additive effects on later-life health outcomes (all-cause mortality, cardiometabolic disease, ADRD)?

2. Do age-specific levels and long-term trajectories of SES attainment and psychosocial resources, and cognitive reserve mediate the associations between dimensions of early adversity and later-life health outcomes?

BEAMS Features Useful for Addressing Life Course Questions

1. Augmenting longitudinal cohort studies with administrative data
2. Harmonization & integrative data analysis to inform replicability
3. Interdisciplinary approach informs integrative science on lifespan health
4. Hybrid design to study processes using different time windows



Mroczek, D.K., Stawski, R.S., Turiano, N.A., Chan, W., Almeida, D.M., Neupert, S.D., & Spiro, A., III. (2013). Emotional reactivity and mortality: longitudinal findings from the va normative aging study. *Journals of Gerontology, Series B: Psychological Sciences and Social Sciences, 70(3)*, 398–406. doi:10.1093/geronb/gbt107. Advance Access publication October 29, 2013

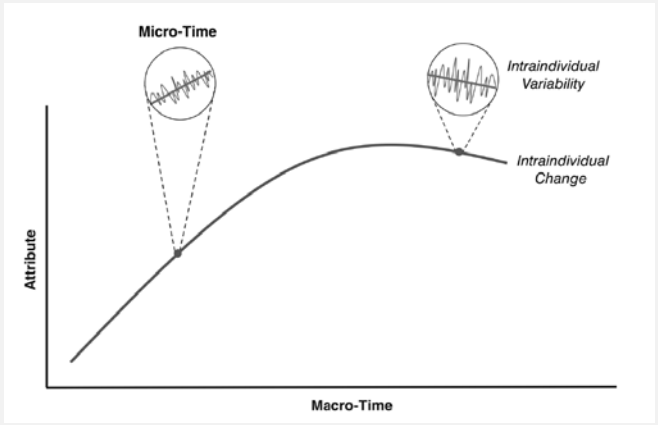
Emotional Reactivity and Mortality: Longitudinal Findings From the VA Normative Aging Study

Daniel K. Mroczek,[1,2] Robert S. Stawski,[3] Nicholas A. Turiano,[4] Wai Chan,[5] David M. Almeida,[6] Shevaun D. Neupert,[7] and Avron Spiro III[8–10]

[1]Department of Psychology, Weinberg College of Arts & Sciences, Northwestern University, Evanston, Illinois.
[2]Department of Medical Social Sciences, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.
[3]School of Social and Behavioral Health Sciences, Oregon State University, Corvallis.
[4]Department of Psychiatry, University of Rochester Medical Center, New York.
[5]Department of Human Development & Family Studies, Purdue University, West Lafayette, Indiana.
[6]Department of Human Development & Family Studies and Center for Healthy Aging, Pennsylvania State University, University Park.
[7]Department of Psychology, North Carolina State University, Raleigh.
[8]Massachusetts Veterans Epidemiology Research & Information Center, VA Boston Healthcare System.
[9]Department of Epidemiology, Boston University School of Public Health, Massachusetts.
[10]Department of Psychiatry, Boston University School of Medicine, Massachusetts.

Objectives. Evidence suggests a predictive association between emotion and mortality risk. However, no study has examined dynamic aspects of emotion in relation to mortality. This study used an index of emotional reactivity, defined as changes in positive or negative affect in response to daily stressors, to predict 10-year survival.

Mroczek et al. (2015) *J Gerontol B Psychol Sci Soc Sci*



Ram & Diehl (2015, chapter) Multiple-time-scale design & analysis

Agenda

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III. Challenges and research opportunities in early adversity and lifespan health

Challenges in Advancing Science on Early Adversity & Lifespan Health

- Parallel to stress-health-aging research
- Difficulties quantifying early adversity ≈ Stress measurement problem

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Frontiers in Neuroendocrinology

journal homepage: www.elsevier.com/locate/yfrne

Review article

More than a feeling: A unified view of stress measurement for population science

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[b] Cousins Center for Psychoneuroimmunology and Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, CA, USA
[c] School of Kinesiology, University of British Columbia, Vancouver, BC, Canada

ARTICLE INFO

Keywords:
Acute stress
Chronic stress
Daily stress
Emotions
Affect
Appraisals
Motivational states
Emotional contagion
Measurement
Allostatic load

ABSTRACT

Stress can influence health throughout the lifespan, yet there is little agreement about what types and aspects of stress matter most for human health and disease. This is in part because "stress" is not a monolithic concept but rather, an emergent process that involves interactions between individual and environmental factors, historical and current events, allostatic states, and psychological and physiological reactivity. Many of these processes alone have been labeled as "stress." Stress science would be further advanced if researchers adopted a common conceptual model that incorporates epidemiological, affective, and psychophysiological perspectives, with more precise language for describing stress measures. We articulate an integrative working model, highlighting how stressor exposures across the life course influence habitual responding and stress reactivity, and how health behaviors interact with stress. We offer a Stress Typology articulating timescales for stress measurement – acute, event-based, daily, and chronic – and more precise language for dimensions of stress measurement.

Key issues:

- No common language of early adversity
- Conflation of heterogeneous constructs, e.g., exposure vs. response ("threat exposure" & "threat appraisal")
- Lack of complex and precise models to capture the phenomenon of early adversity & its health impact

Also see: https://www.stressmeasurement.org/

Framework for Studying Early Adversity & Lifespan Health (I)

Exposure

- Systematic quantification of early adversity exposures
  - Domains, e
    - SES
    - Environ
    - Psycho social i evaluat
  - Characteris
    - Duratio (daily?
    - Freq, int
    - Threat vs. deprivation
- Characterize exposure co-occurrence

Response

- Within-person response across levels
  - Recovery
  - Habituation
- Timescale

Health outcomes

- Multiple domains
  - m, e.g.:
  - ic
  - ion (obesity, istance, etc.)
  - h depression
  - nes, e.g.:
  - e death
  - mes, e.g.,:
  - pan"
  - Cardiovascular health
  - Positive psychological well-being

Common elements (research tasks) across categories:

- Construct definition & operationalization
- Measurement development
- Quantify distributions across populations
- Examine co-occurrences or causal associations among constructs in the same category

Framework for Studying Early Adversity & Lifespan Health (II)

Exposure

- Systematic quantification of early adversity exposures
  - Domains, e.g.:
    - SES
    - Environmental
    - Psychological (e.g., social isolation, evaluative)
  - Characteristics, e.g.:
    - Duration & timescale (daily? chronic?)
    - Freq, intensity
    - Threat vs. deprivation
- Characterize exposure co-occurrence

Response

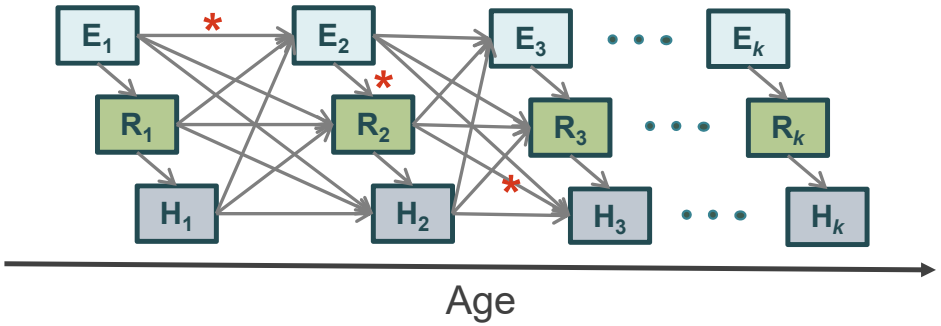
- Within-person response across levels:
  - Psych (cog, affective)
  - Neural
  - Physiological
  - Genetic & cellular
  - Behavioral
  - *Cross-level interactions / feedback loops*
- Response patterns, e.g.:
  - Anticipation
  - Reactivity
  - Recovery
  - Habituation
- Timescale

Health outcomes

- Multiple domains
- Shorter-term, e.g.:
  - Physiologic dysregulation (obesity, insulin resistance, etc.)
  - Past-month depression
- "Hard" outcomes, e.g.:
  - Diseases
  - Disability
  - Premature death
- Positive outcomes, e.g.,:
  - "Healthspan"
  - Cardiovascular health
  - Positive psychological well-being

Framework for Studying Early Adversity & Lifespan Health (III)

- Bidirectional influences among exposure, response, and health outcomes
- Contextual factors: Sex, Cohort, geography, race/ethnicity
- Protective factors (e.g., cognitive enrichment) & effect modifiers
- Model of risk transmission over developmental span
- Analytic challenges: causality, multiple time scales, small effects from chain-of-risk w multiple mediators (*)
- Cross-study harmonization & replication



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