Identifying Midlife Social Exposures that Might Modify Risk for Cognitive Impairment Associated with Early Life Disadvantage Workshop

Session 4: Social and Health Policies

August 29, 2024

David H. Rehkopf, Associate Professor

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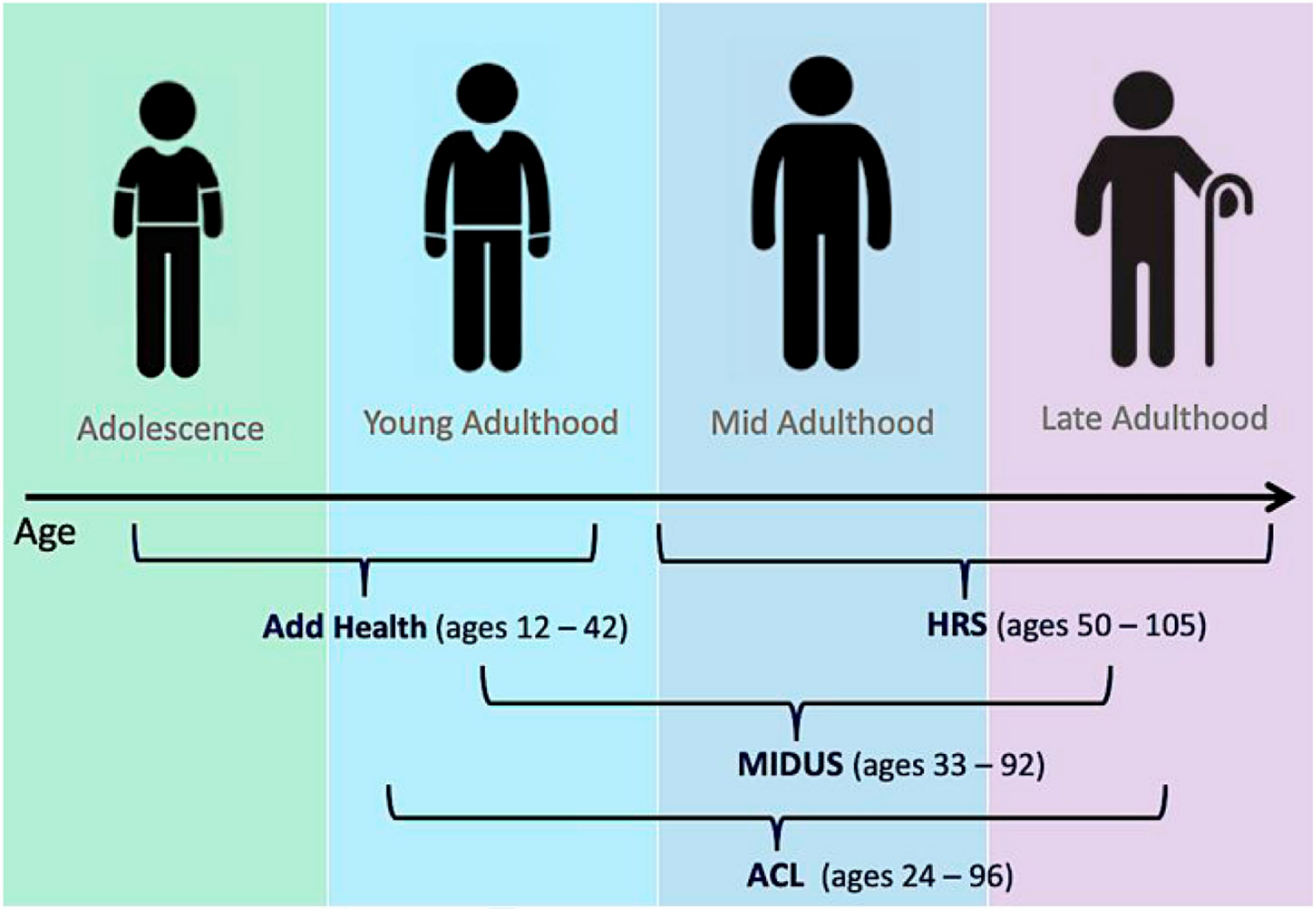
Departments of Epidemiology and Population Health, Medicine, Pediatrics, Health Policy, Sociology, Stanford University

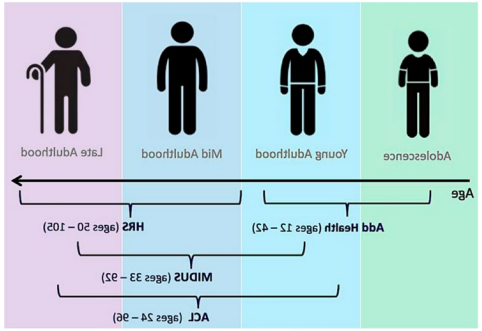


Yang *et al* Journal of Aging and Health, 2023

Why don't we know more about this relationship across the life course?

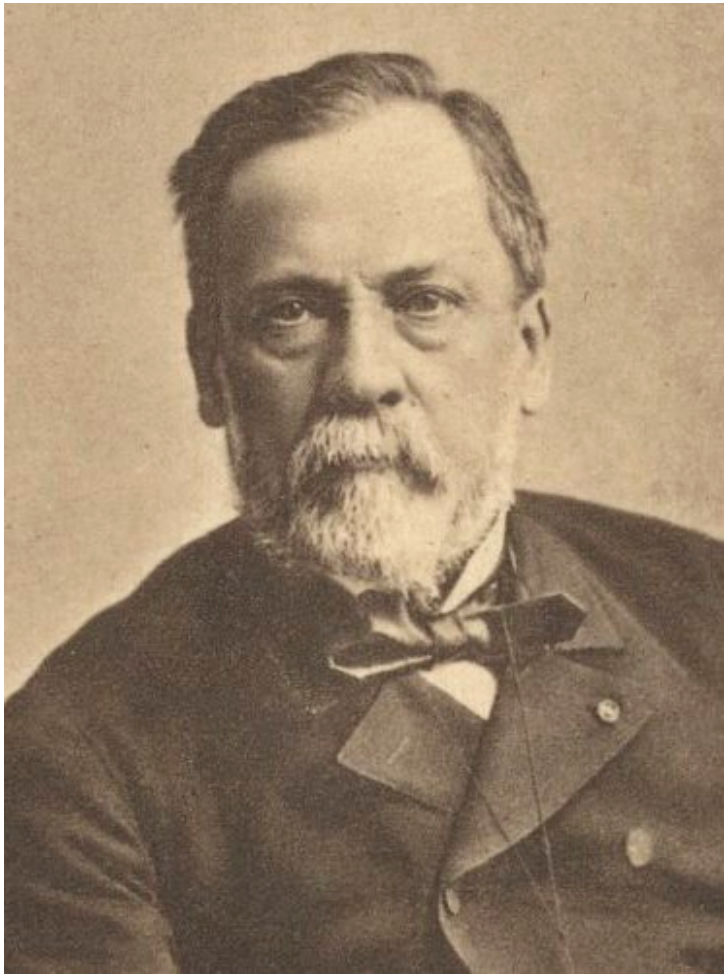
1. Dominance of both proximal and early life factors in theory

2. Smallish sample sizes for social and economic policy analysis

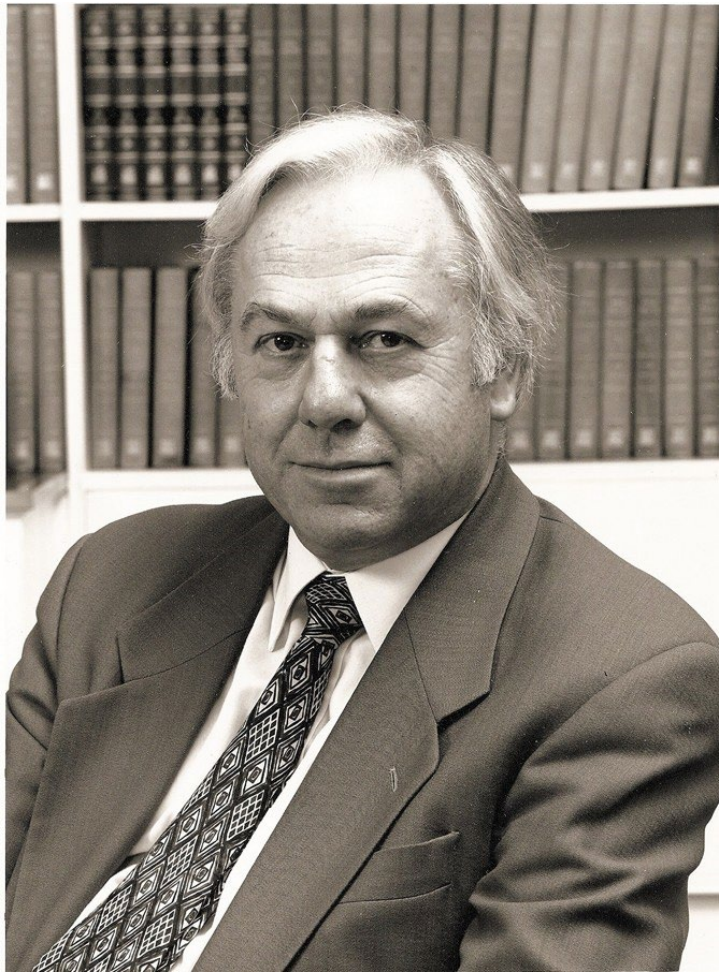


3. Difficulties in measurement due to timing of exposures and outcomes

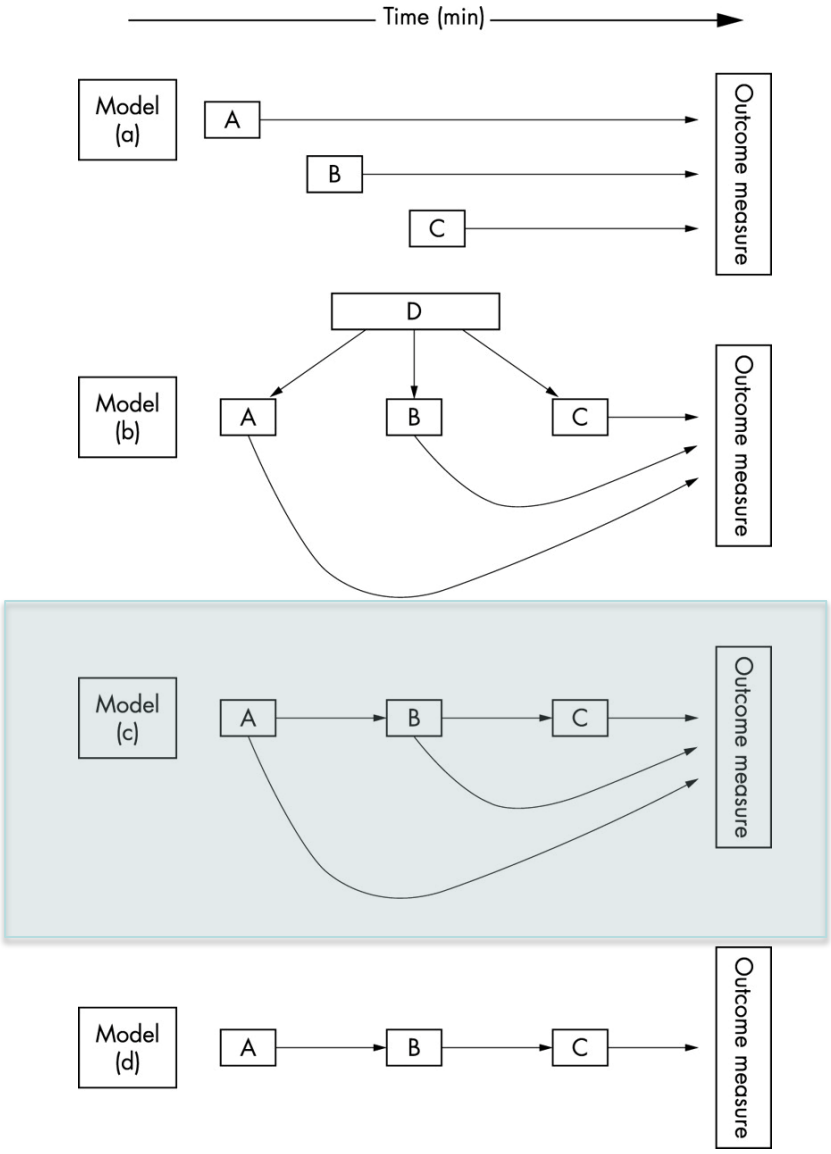
1. Dominance of both proximal and early life factors in theory



versus



But the actual evidence…



Socioeconomic trajectories across the life course and health outcomes in midlife: evidence for the accumulation hypothesis?

Archana Singh-Manoux, Jane E Ferrie, Tarani Chandola and Michael Marmot

Psychological Medicine

cambridge.org/psm

Original Article

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Key words:
Childhood adversity
course; recency; acc
psychopathology

What life course theoretical models best explain the relationship between exposure to childhood adversity and psychopathology symptoms: recency, accumulation, or sensitive periods?

Erin C. Dunn[1,2,3], Thomas W. Soare[1,2,3], Miriam R. Raffeld[1], Daniel S. Busso[1,4], Katherine M. Crawford[1], Kathryn A. Davis[1], Virginia A. Fisher[1,5], Natalie Slopen[6], Andrew D.A.C. Smith[7], Henning Tiemeier[8] and Ezra S. Susser[9,10]

[1]Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA; [2]Department of Psychiatry,

Article

Socioeconomic Status Across the Life Course and Cognitive Function Among Older Adults: An Examination of the Latency, Pathways, and Accumulation Hypotheses

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DOI: 10.1177/0898264315585504
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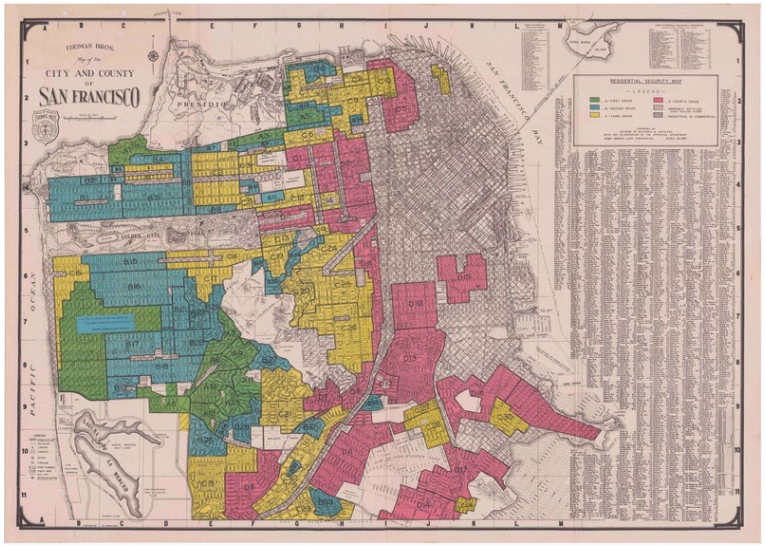
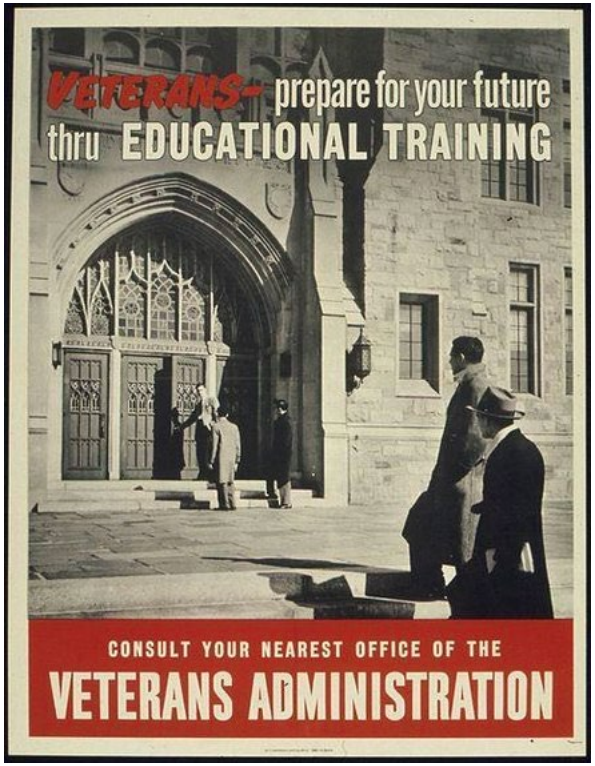
Jiyoung Lyu, PhD[1] and Jeffrey A. Burr, PhD[2]

2. Smallish sample sizes for policy analysis

Federal Programs and race





- Range of emergency work relief programs.
- WPA was the largest, at peak, it employed about three million individuals.
- Between 1935 and 1943 provided employment for 8.5 million individuals.
- 1940 population of the U.S. was 132 million.

Demography (2022) 59(4):1489–1516
DOI 10.1215/00703370-10111856

Published online: 19 July 2022

Demography. 2022 59(4):1489-1516.

Long-Term Effects of Local-Area New Deal Work Relief in Childhood on Educational, Economic, and Health Outcomes Over the Life Course: Evidence From the Wisconsin Longitudinal Study

Sepideh Modrek, Evan Roberts, John Robert Warren, and Da

Table 3 Analytic sample summary statistics of outcomes derived from the WL indicated)

	Number of Observations
Parental Income, Adolescent Cognition, and Education Outcomes	
Parental income, 1957–1960 (from tax records)	4,692
Standardized freshman/junior IQ (1954/1956; $)	5,303
High school rank (1957)	4,937
% Bachelor's degree or higher	4,000
% Attended any college	4,652
Early Adulthood Work Outcomes (1974)	
% In labor force	4,971
Graduate wages ($)[a]	4,721
Midlife BMI and Health Behavior Outcomes	
% BMI >35 (1992)	5,203
% Ever smoked regularly (2004)	3,724
Alcohol problem (range, 0–5; 2004)	3,913
Late-Life Cognitive Measures	
Wechsler Adult Intelligence Scale	2,772
Standardized language/executive function (2004)	3,767
Standardized memory (2004)	2,994
Standardized language/executive function (2011)	3,161
Standardized memory (2011)	2,508
Dead at Follow-up Through 2019	
% Male	2,521
% Female	2,782

[a] Top-coded at 10,000. Sample in the two-part model.

Table 7 Estimated effects of area-level emergency employment activity in 1940 on late-life cognitive summary outcomes (standardized score from the Wechsler Adult Intelligence Scale)

	1992		2004		2011	
	(1)	(2)	(3)	(4)	(5)	(6)
Individual Level						
Female	–0.102	0.412	–0.007	0.025	–0.086*	0.015
	[0.102]	[0.291]	[0.036]	[0.111]	[0.038]	[0.103]
Father's Work Status (ref. = unemployed)						
Regular work	0.009	0.018	0.084	0.080	0.012	0.004
	[0.298]	[0.298]	[0.103]	[0.103]	[0.107]	[0.107]
Emergency employment	–0.444	–0.428	–0.035	–0.045	–0.142	–0.155
	[0.360]	[0.360]	[0.121]	[0.122]	[0.124]	[0.124]
Not in labor force	0.441	0.453	0.104	0.095	–0.040	–0.049
	[0.454]	[0.454]	[0.180]	[0.180]	[0.171]	[0.172]
ED Level (ref. = Q1)						
Q2	0.251	0.416	0.064	0.072	0.077	0.103
	[0.179]	[0.278]	[0.067]	[0.105]	[0.069]	[0.104]
Q3	0.353†	0.745**	0.142*	0.199†	0.130†	0.217*
	[0.186]	[0.274]	[0.069]	[0.102]	[0.069]	[0.100]
Q4	0.215	0.619*	0.048	0.038	0.038	0.063
	[0.194]	[0.280]	[0.073]	[0.108]	[0.070]	[0.101]
Q5	0.245	0.554†	0.145†	0.170	0.109	0.237*
	[0.218]	[0.301]	[0.085]	[0.118]	[0.083]	[0.113]
Emergency Employment Activity × Gender (ref. = Q1 × female)						
Q2 × female		–0.275		–0.013		–0.041
		[0.368]		[0.136]		[0.130]
Q3 × female		–0.717*		–0.108		–0.160
		[0.364]		[0.134]		[0.136]
Q4 × female		–0.728*		0.020		–0.042
		[0.356]		[0.133]		[0.126]
Q5 × female		–0.558		–0.045		–0.233†
		[0.367]		[0.138]		[0.135]
Number of Observations	2,772	2,772	2,772	2,772	2,772	2,772
R^2	.034	.036	.029	.03	.032	.033

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	[0.298]	[0.298]	[0.103]	[0.103]	[0.107]	[0.107]
Emergency employment	–0.444	–0.428	–0.035	–0.045	–0.142	–0.155
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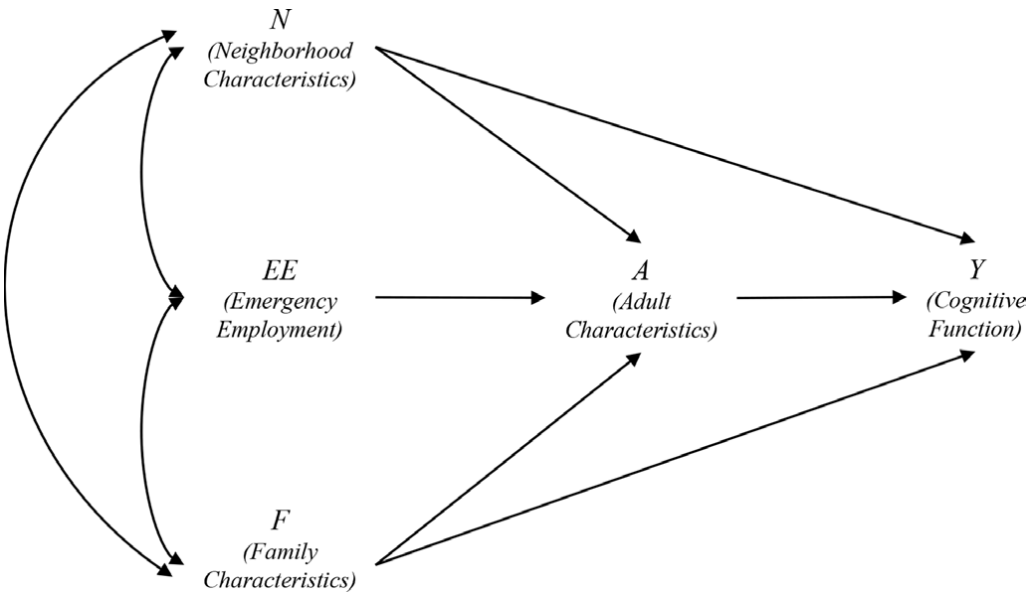
		[0.367]		[0.138]		[0.135]
Number of Observations	2,772	2,772	2,772	2,772	2,772	2,772
R^2	.034	.036	.029	.03	.032	.033

Associations of local area level new deal employment in childhood with late life cognition: evidence from the census-linked health and retirement study

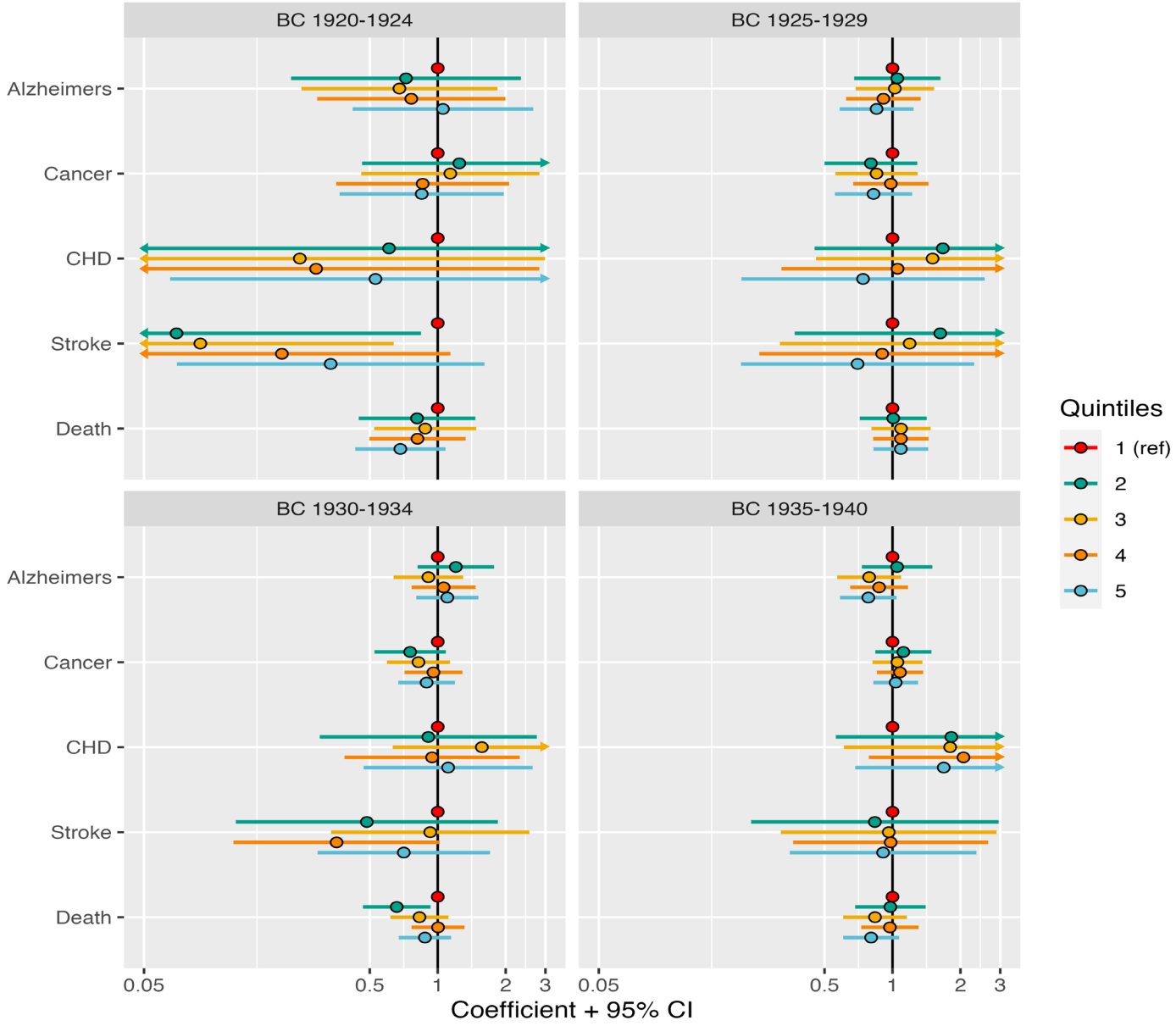
Mark Lee [1], Amal Harrati [2], David H. Rehkopf [3], Sepideh Modrek [4]



Journal of Epidemiology and Community Health. doi:10.1136/jech-2022-219259.

Table 3 Estimated effects of area (enumeration district) level emergency employment (from 1940 census) on baseline cognition and cognitive decline (1998–2016): Health and Retirement Study (N=5095)

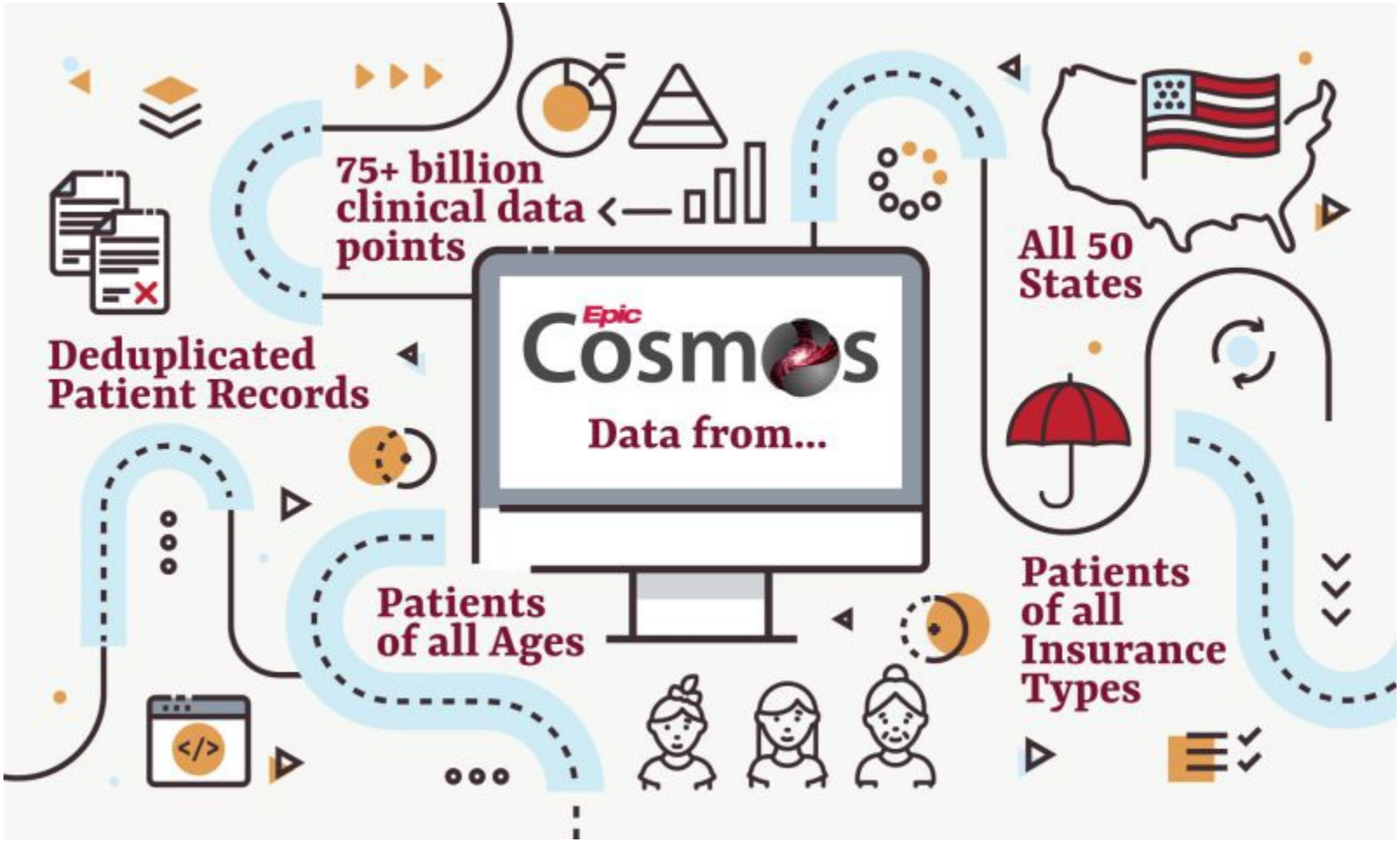
	Model 1		Model 2		Model 3		Model 4	
Variable	**B**	**95% CI**	**B**	**95% CI**	**B**	**95% CI**	**B**	**95% CI**
Time	−0.062	−0.066 to −0.057	−0.062	−0.066 to −0.057	−0.062	−0.067 to −0.057	−0.062	−0.067 to −0.058
ED-level emergency employment								
Q1 (lowest)	0	Ref	0	Ref	0	Ref	0	Ref
Q2	0.030	−0.056 to 0.115	0.017	−0.066 to 0.101	0.007	−0.073 to 0.087	0.012	−0.066 to 0.090
Q3	0.064	−0.019 to 0.146	0.092	0.011 to 0.173	0.060	−0.014 to 0.135	0.073	0.000 to 0.147
Q4	0.000	−0.086 to 0.086	0.059	−0.027 to 0.146	0.025	−0.054 to 0.104	0.037	−0.040 to 0.115
Q5 (highest)	−0.066	−0.152 to 0.019	0.070	−0.022 to 0.161	0.015	−0.068 to 0.099	0.040	−0.042 to 0.122
ED-level emergency employment X time								
Q1 X time	0	Ref	0	Ref	0	Ref	0	Ref
Q2 X time	−0.003	−0.010 to 0.004	−0.003	−0.010 to 0.004	−0.002	−0.009 to 0.004	−0.003	−0.009 to 0.004
Q3 X time	−0.005	−0.011 to 0.002	−0.005	−0.011 to 0.002	−0.005	−0.011 to 0.002	−0.005	−0.011 to 0.002
Q4 X time	−0.003	−0.010 to 0.003	−0.003	−0.010 to 0.003	−0.003	−0.010 to 0.003	−0.003	−0.010 to 0.003
Q5 X time	−0.003	−0.010 to 0.004	−0.003	−0.010 to 0.004	−0.003	−0.010 to 0.004	−0.003	−0.010 to 0.004



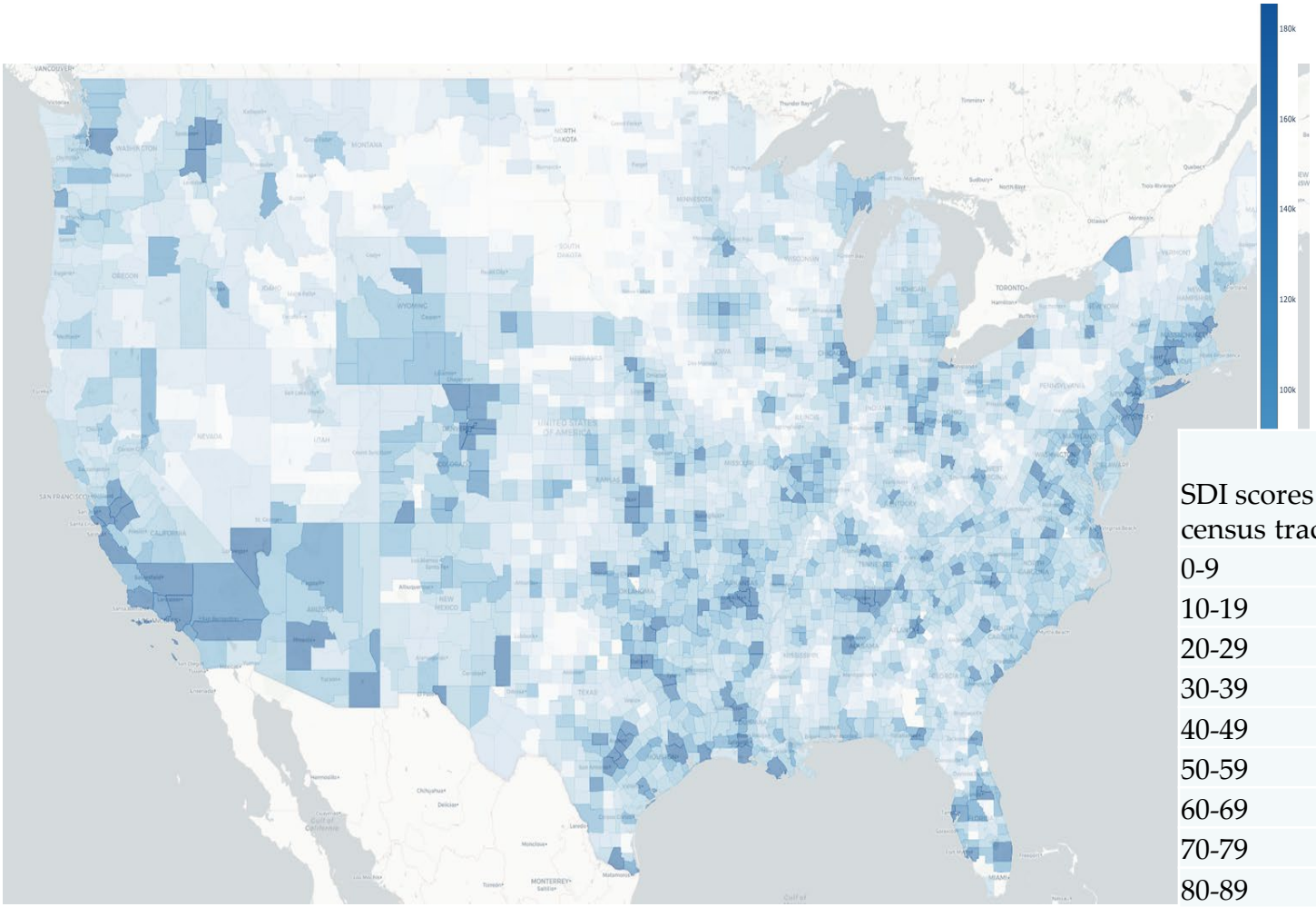
Meta-analyzing HRS and Women's Health Initiative data

Rehkopf *et al.* PAA Poster 2024

Possibilities with Electronic Health Record Data

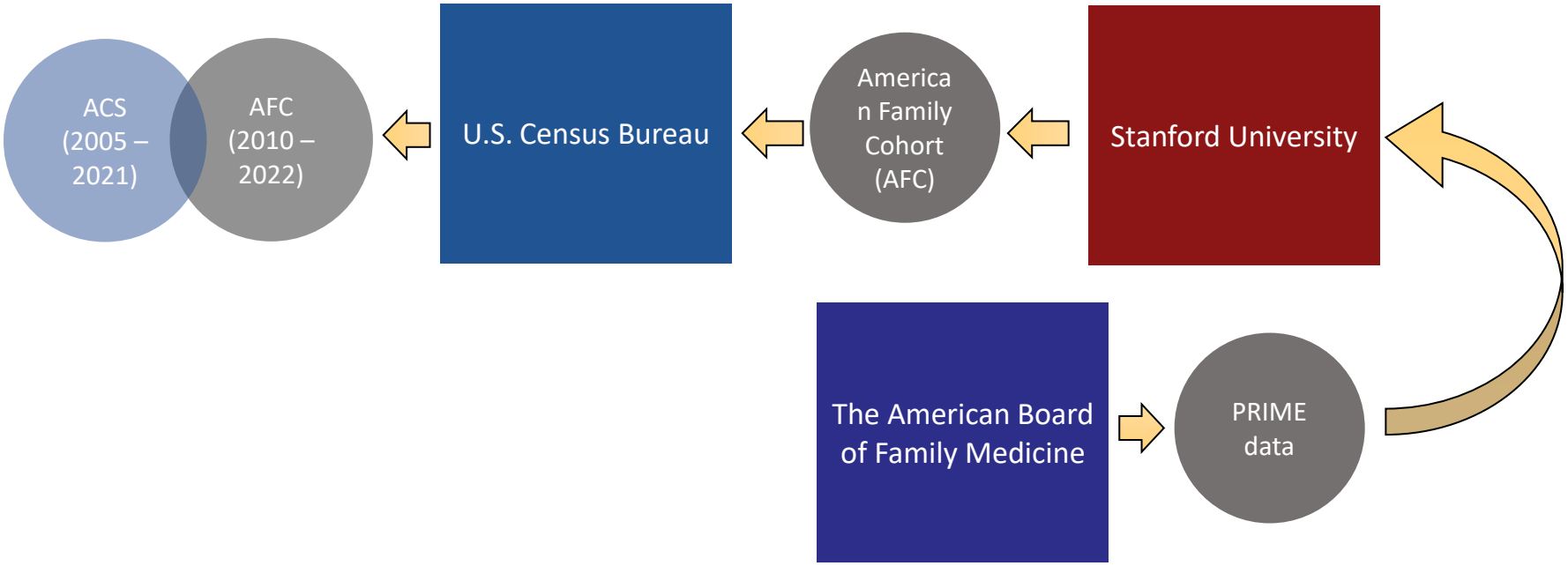


Possibilities with Electronic Health Record Data



SDI scores at census tract level	% patients
0-9	10
10-19	10
20-29	11
30-39	11
40-49	12
50-59	12
60-69	11
70-79	10
80-89	8
90-100	6

Individual level linkage of Electronic Health Record data to life course Census Data

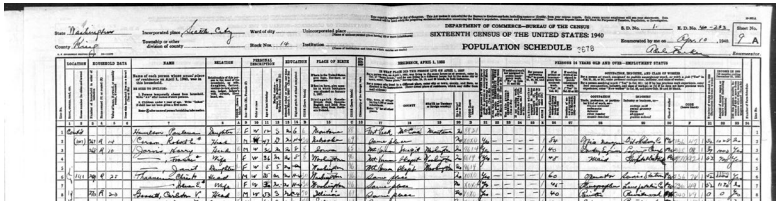


Limburg *et al.* PAA talk 2024, under review

3. Difficulties in measurement due to timing of exposures and outcome

Data linkage is essential

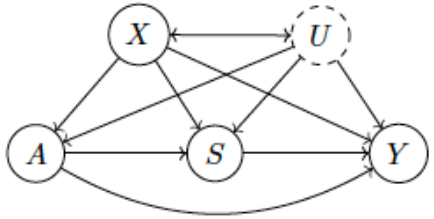
1. Probabilistic linkage



2. Exact matching

United States™ Census Bureau

3. Surrogate outcomes



(a) Observational data.

STATISTICS IN MEDICINE, VOL. 8, 431–440 (1989)

SURROGATE ENDPOINTS IN CLINICAL TRIALS: DEFINITION AND OPERATIONAL CRITERIA

ROSS L. PRENTICE

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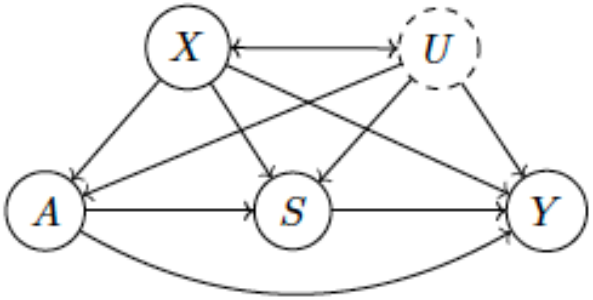
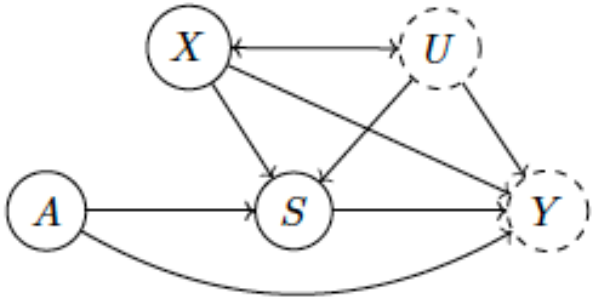
SUMMARY

I discuss the idea of using surrogate endpoints in the context of clinical trials to compare two or more treatments or interventions in respect to some 'true' endpoint, typically a disease occurrence. In order that treatment comparison based on a surrogate response variable have a meaningful implication for the corresponding true endpoint treatment comparison, a rather restrictive criterion is proposed for use of the adjective 'surrogate'. Specifically, I propose that a surrogate for a true endpoint yield a valid test of the null hypothesis of no association between treatment and the true response. This criterion essentially requires the surrogate variable to 'capture' any relationship between the treatment and the true endpoint, a notion that can be operationalized by requiring the true endpoint rate at any follow-up time to be independent of treatment, given the preceding history of the surrogate variable. I then discuss this operational criterion in the examples of the accompanying papers[1–3] and in the setting of trials aimed at the primary and secondary prevention of cancer.

KEY WORDS Clinical trials Disease prevention trials Hazard rates Surrogate endpoints Therapeutic trials



(a) Observational data.



(b) experimental data.

Figure 1: Causal diagrams for observational and experimental data with persistent confounders. Here A denotes the treatment, S denotes (multiple) short-term outcomes, Y denotes the long-term outcome, X denotes covariates, and U denotes unobserved confounders. Confounders U in both samples and the long-term outcome Y in the experimental data are unobserved, so they are indicated by dashed circles. Note that unobserved confounders U can simultaneously affect short-term outcomes S and the long-term outcome Y.

Imbens *et al.* 2024

Table 1: OBSERVATION SCHEME: ✓ IS OBSERVED, ? IS MISSING

Units	Sample P_i	Treatment W_i	Long-Term Outcome Y_i	Surrogate S_i	Pretreatment Variables X_i
1 to N_{E}	E	✓	?	✓	✓
$N_{\mathrm{E}}+1$ to $N_{\mathrm{E}}+N_{\mathrm{O}}$	O	?	✓	✓	✓

Athey *et al.* 2024

NBER WORKING PAPER SERIES

THE SURROGATE INDEX: COMBINING SHORT-TERM PROXIES TO ESTIMATE LONG-TERM TREATMENT EFFECTS MORE RAPIDLY AND PRECISELY

Susan Athey
Raj Chetty
Guido W. Imbens
Hyunseung Kang

Working Paper 26463
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On the Role of Surrogates in the Efficient Estimation of Treatment Effects with Limited Outcome Data

Nathan Kallus[1]* Xiaojie Mao[2]*

[1]Cornell University, New York, NY, USA; [2]Tsinghua University, Beijing, China

Abstract

In many experiments and observational studies, the outcome of interest is often difficult or expensive to observe, reducing effective sample sizes for estimating average treatment effects (ATEs) even when identifiable. We study how incorporating data on units for which only surrogate outcomes not of primary interest are observed can increase the precision of ATE estimation. We refrain from imposing stringent surrogacy conditions, which permit surrogates as perfect replacements for the target outcome. Instead, we supplement the available, albeit limited, observations of the target outcome (which by themselves identify the ATE) with abundant observations of surrogate outcomes, without any assumptions beyond random assignment and missingness and corresponding overlap conditions. To quantify the potential gains, we derive the difference in efficiency bounds on ATE estimation with and without surrogates, both when an overwhelming or comparable number of units have missing outcomes. We develop robust ATE estimation and inference methods that realize these efficiency gains. We empirically demonstrate the gains by studying long-term-earning effects of job training.

emiparametric

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RESEARCH ARTICLE

Statistics in Medicine WILEY

Estimation of the proportion of treatment effect explained by a high-dimensional surrogate

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Abstract

Clinical studies examining the effectiveness of a treatment with respect to some primary outcome often require long-term follow-up of patients and/or costly or burdensome measurements of the primary outcome of interest. Identifying a surrogate marker for the primary outcome of interest may allow one to evaluate a treatment effect with less follow-up time, less cost, or less burden. While much clinical and statistical work has focused on identifying and validating surrogate markers, available approaches tend to focus on settings in which only a single surrogate marker is of interest. Limited work has been done to accommodate the high-dimensional surrogate marker setting where the number of potential surrogates is greater than the sample size. In this article, we develop methods to

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A SURROGATE ENDPOINT BASED PROVISIONAL APPROVAL CAUSAL ROADMAP

A PREPRINT

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Full Length Article

Long-term causal effects estimation via latent surrogates representation learning

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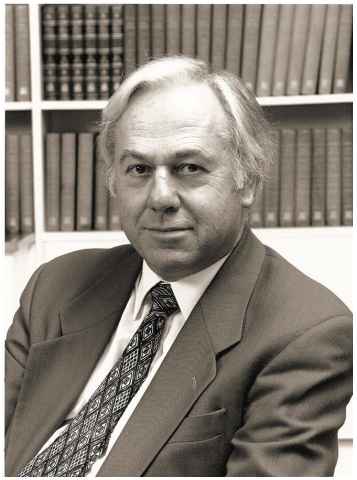
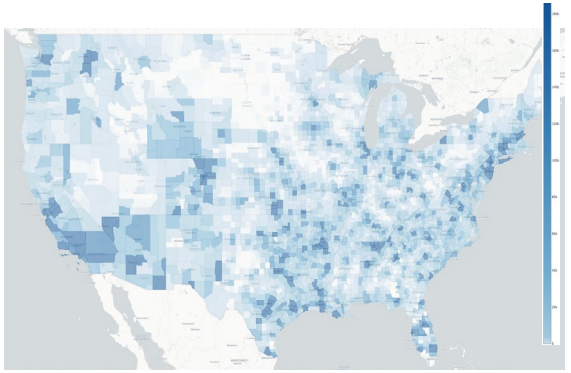
ARTICLE INFO ABSTRACT

Summary

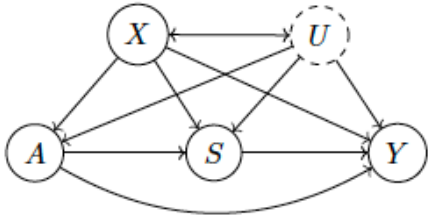


1. Dominance of both proximal and early life factors in theory



2. Smallish sample sizes for social and economic policy analysis

3. Difficulties in measurement due to timing of exposures and outcomes



(a) Observational data.

Thank you.

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