Environmental considerations in mental health research
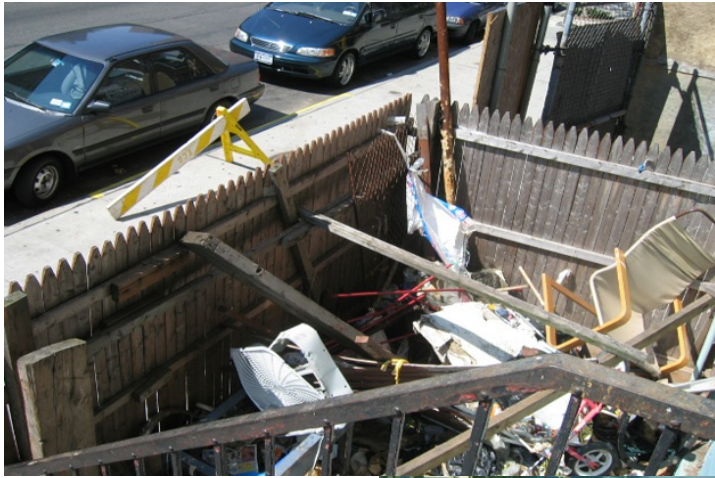
Sandro Galea

Advancing Our Understanding Of The Brain

Why might we think the environment matters for mental health?
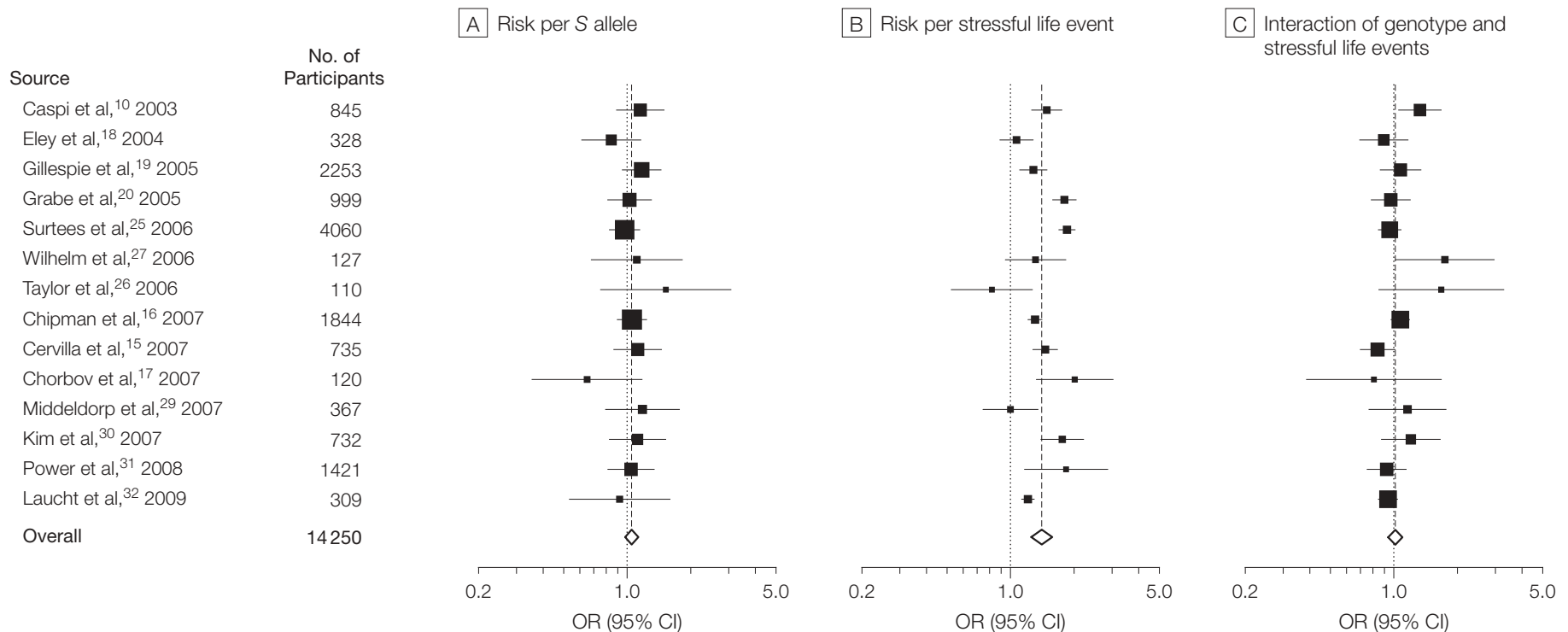
Intuition

Concepts

Interaction Between the Serotonin Transporter Gene (*5-HTTLPR*), Stressful Life Events, and Risk of Depression
A Meta-analysis

Figure 2. Logistic Regression Analyses of Risk of Depression for 14 Studies

Source	No. of Participants
Caspi et al,[10] 2003	845
Eley et al,[18] 2004	328
Gillespie et al,[19] 2005	2253
Grabe et al,[20] 2005	999
Surtees et al,[25] 2006	4060
Wilhelm et al,[27] 2006	127
Taylor et al,[26] 2006	110
Chipman et al,[16] 2007	1844
Cervilla et al,[15] 2007	735
Chorbov et al,[17] 2007	120
Middeldorp et al,[29] 2007	367
Kim et al,[30] 2007	732
Power et al,[31] 2008	1421
Laucht et al,[32] 2009	309
Overall	14 250

A. Risk per *S* allele — OR (95% CI)
B. Risk per stressful life event — OR (95% CI)
C. Interaction of genotype and stressful life events — OR (95% CI)

The boxes and lines indicate the odds ratios (ORs) and their 95% confidence intervals (CIs) on a log scale for each study. The size of the box indicates the relative weight of each estimate.

Risch et al., *JAMA* (2009) 301: 2462-71

npg

ORIGINAL ARTICLE

A mega-analysis of genome-wide association studies for major depressive disorder

Major Depressive Disorder Working Group of the Psychiatric GWAS Consortium[1]

Prior genome-wide association studies (GWAS) of major depressive disorder (MDD) have met with limited success. We sought to increase statistical power to detect disease loci by conducting a GWAS mega-analysis for MDD. In the MDD discovery phase, we analyzed more than 1.2 million autosomal and X chromosome single-nucleotide polymorphisms (SNPs) in 18 759 independent and unrelated subjects of recent European ancestry (9240 MDD cases and 9519 controls). In the MDD replication phase, we evaluated 554 SNPs in independent samples (6783 MDD cases and 50 695 controls). We also conducted a cross-disorder meta-analysis using 819 autosomal SNPs with $P < 0.0001$ for either MDD or the Psychiatric GWAS Consortium

" Although this is the largest genome-wide analysis of MDD yet conducted…we were unable to identify robust and replicable findings "
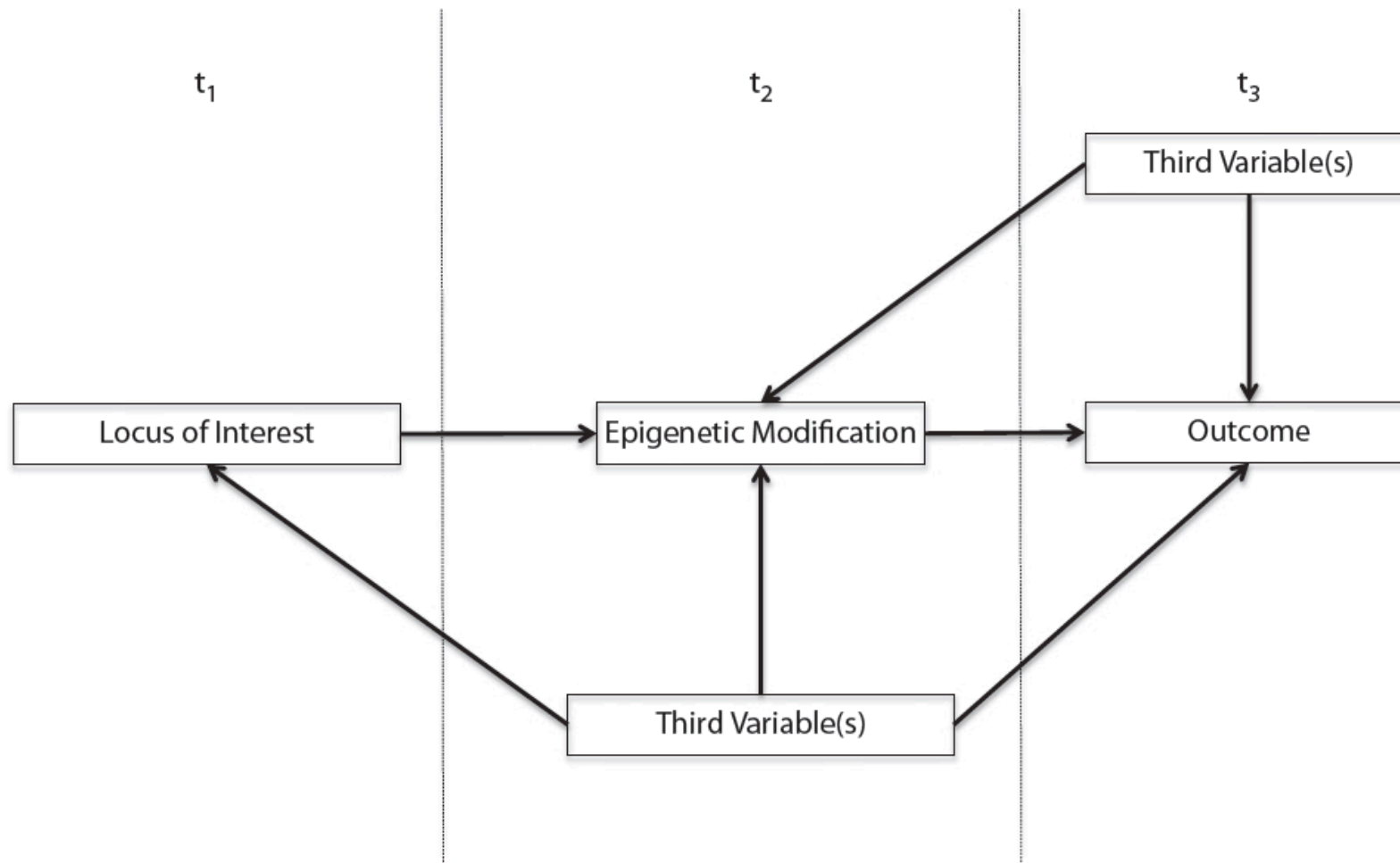
Note. t_1 = time 1; t_2 = time 2; t_3 = time 3. Support of epigenetic hypotheses requires measurement at three time points, and third variables that might confound relationships among loci, epigenetic modification, and outcomes should be measured at the second and third time points and adjusted for appropriately in analyses.

FIGURE 1—Epigenetic modification as a mediator between genetic factors and outcomes and associated confounders.

El-Sayed AM, Koenen KC, Galea S. Rethinking our public health genetics research paradigm. American Journal of Public Health. 2013;103(S1): S14-S18. PMID: 23927512. PMCID: PMC3786747. http://dx.doi.org/10.2105%2FAJPH.2012.301127

Evidence

1. Pathogens

2. Disruptions

3. Form

1. Environmental pathogens

Figure 2. Association of Childhood Blood Lead Level at 11 Years of Age With Adult General Psychopathology at 38 Years of Age (Unadjusted for Covariates)
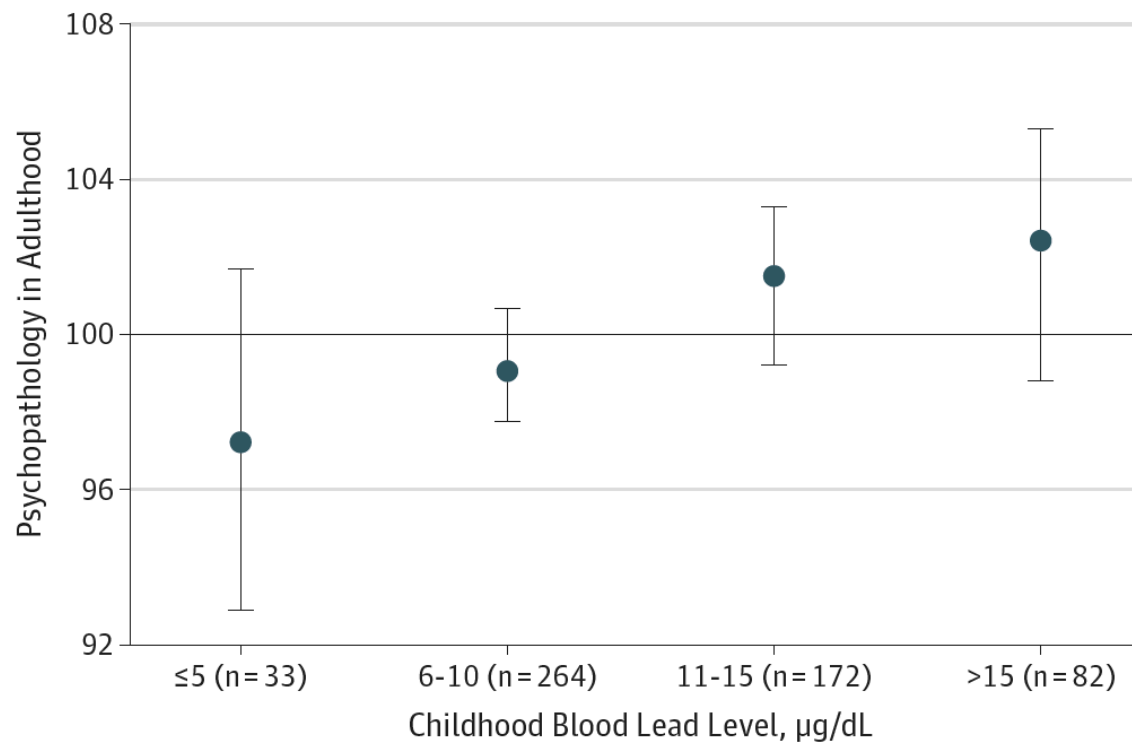
The mean general psychopathology scores (circles) in adulthood with 95% CIs (error bars) by childhood blood lead level are shown. Each 5-µg/dL–higher level of blood lead in childhood was associated with an additional 1.49-point higher score (95% CI, 0.22-2.77; P = .02) in adult general psychopathology on a scale standardized to a mean (SD) of 100 (15) (horizontal line). Of the 579 study members with childhood blood lead level measured, 551 (95.2%) also had present data on all the covariates and the psychopathology outcome measures.

Results: The results of all selected studies showed statistically significant associations between daily hospital admissions and ED visits for mental disorders and daily levels of some or all air pollutants considered, including particulate matter (PM) of variable sizes (in micrometers given in subscripts; $PM_{2.5}$ and PM_{10}), sulfur dioxide, carbon monoxide, nitrogen oxide, and ozone. The strongest and more consistent evidence across studies was found for $PM_{2.5}$ and PM_{10}.
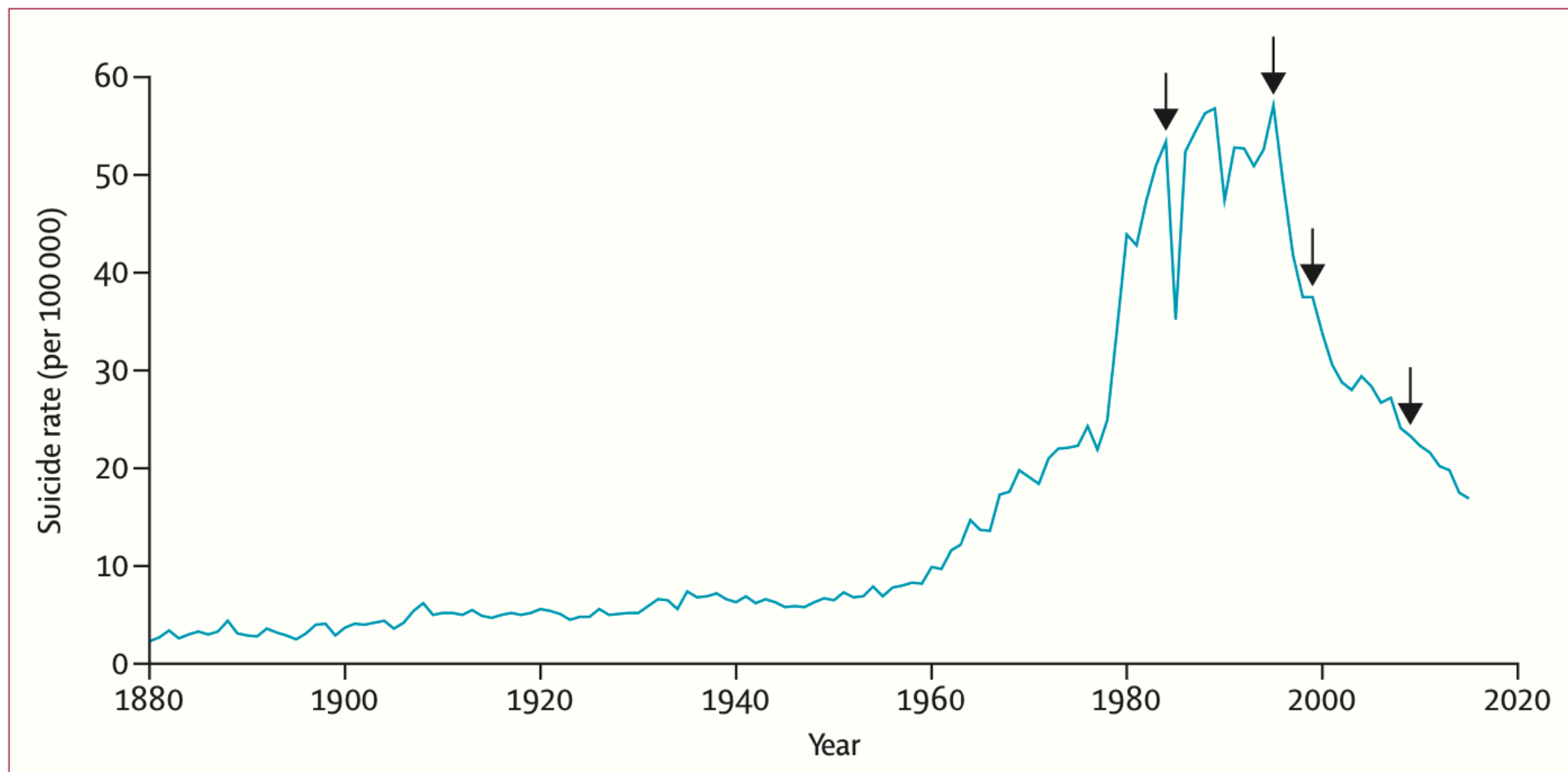
Figure 1: Overall suicide rate in Sri Lanka, 1880–2015

Arrows show timing of pesticide bans in 1984 (parathion and methylparathion), 1995 (all remaining WHO class 1 toxicity pesticides, including methamidophos and monocrotophos), 1998 (endosulfan), and 2008 (dimethoate, fenthion, and paraquat). Suicide data were obtained from police records. Reproduced with permission from Knipe et al.[17]
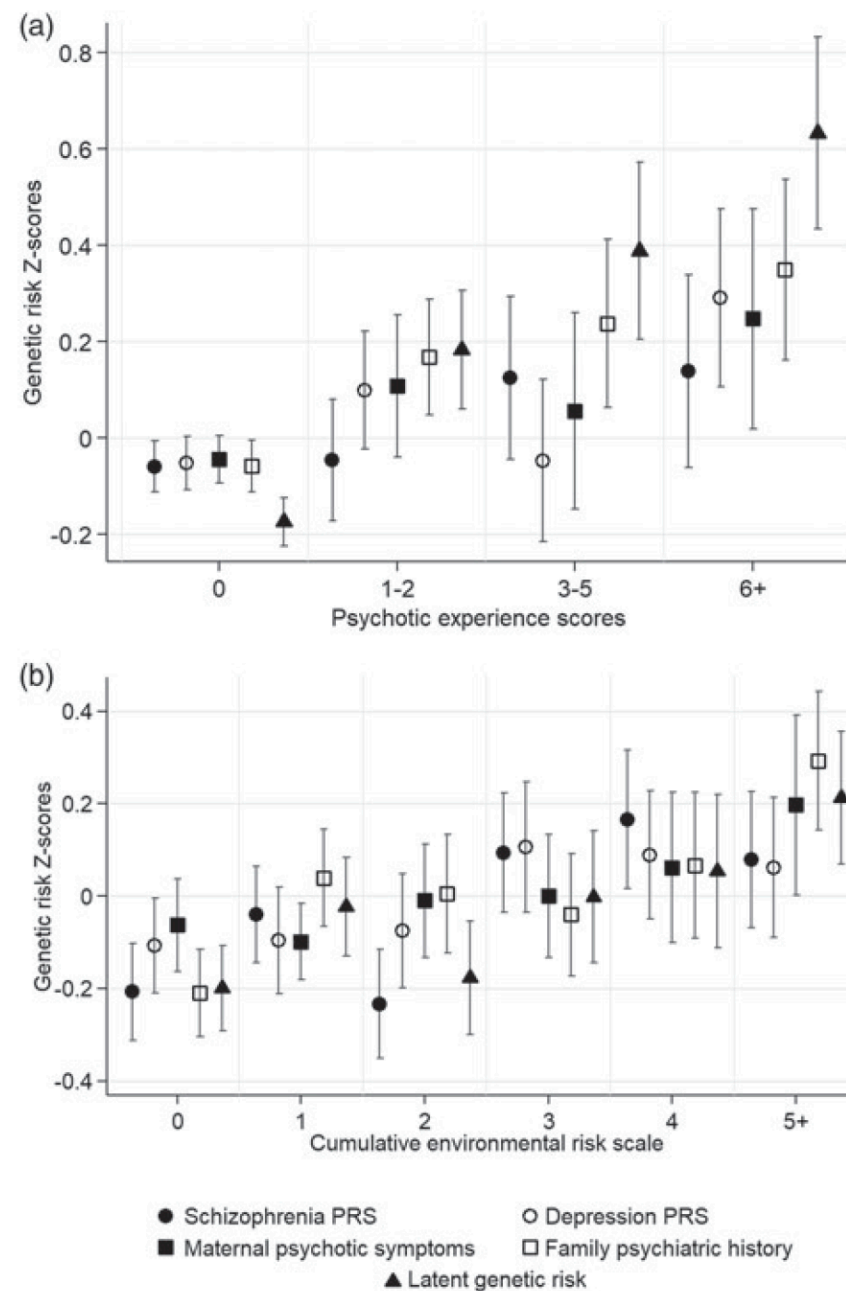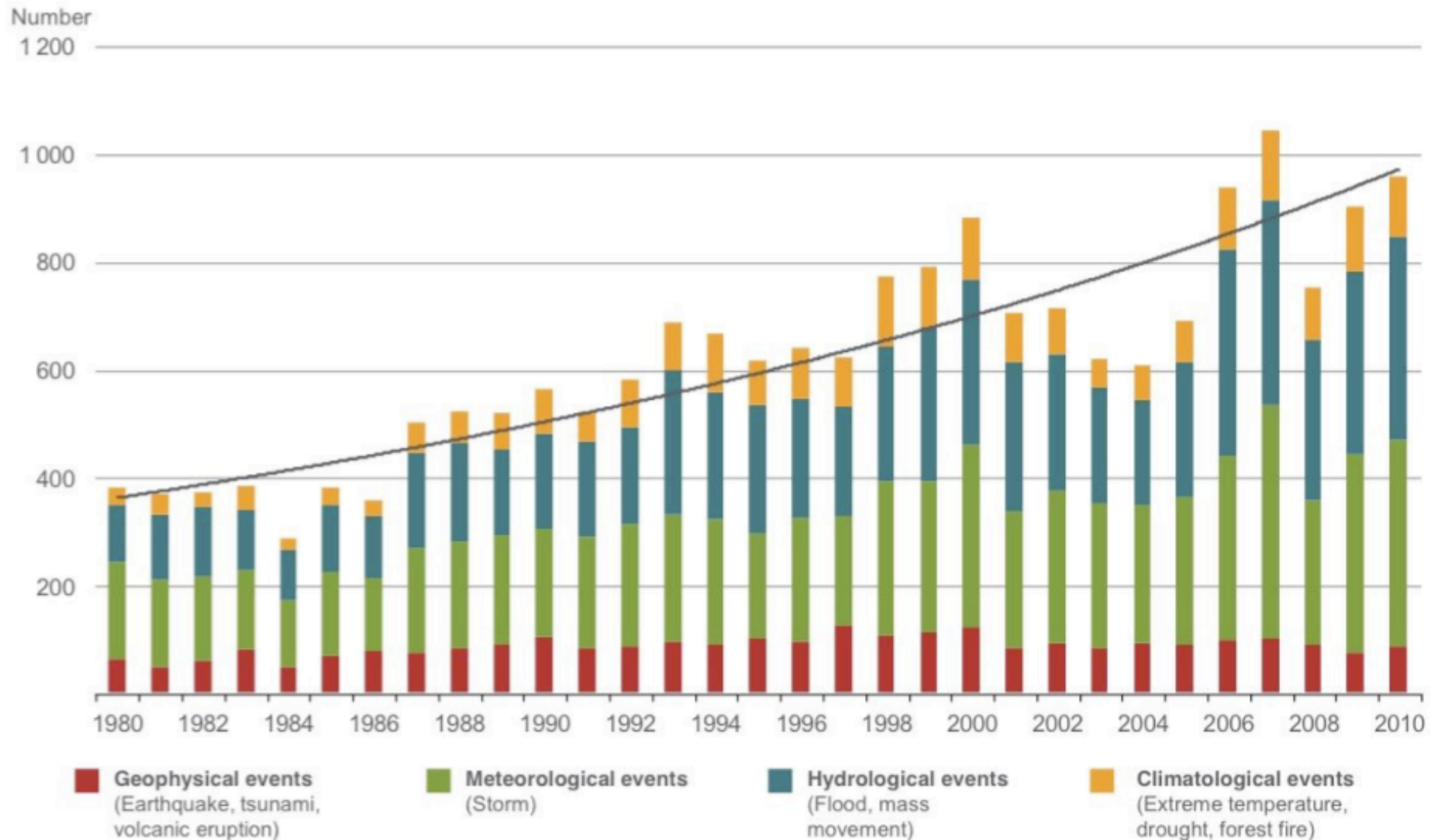
Fig. 2. Genetic risk Z-scores and 95% confidence intervals (indicated by double-headed lines) across (a) adolescent psychotic experiences scores, and (b) the cumulative environmental risk scale. Note: PRS, polygenic risk score.
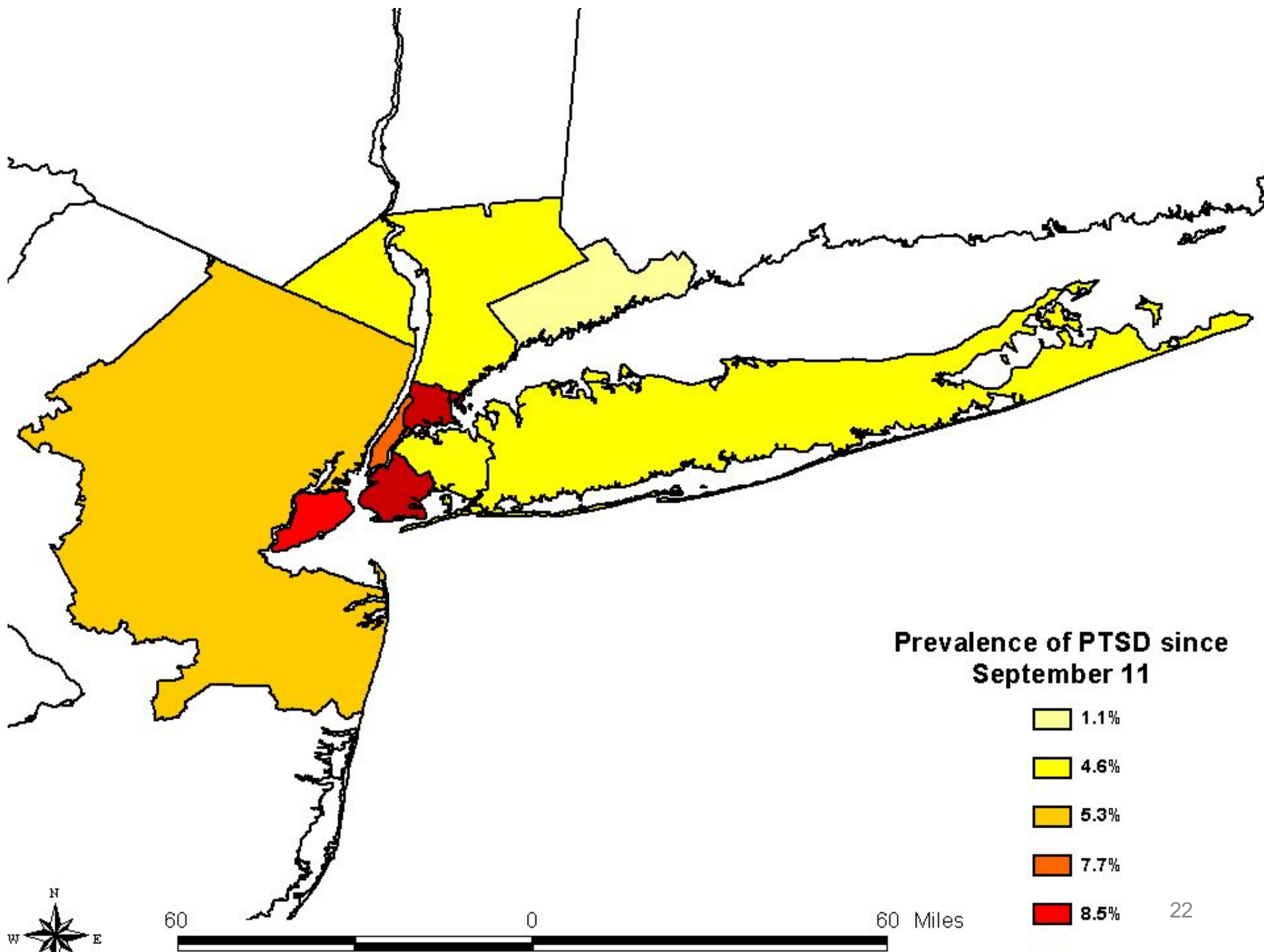
2. Environmental disruptions

" A traumatic event is an experience that causes physical, emotional, psychological distress, or harm. It is an event that is perceived and experienced as a threat to one's safety or to the stability of one's world. "

http://www.nlm.nih.gov/medlineplus/ency/article/001924.htm

Levetown M. Communicating with children and families: from everyday interactions to skill in conveying distressing information. Pediatrics. 2008;121:e1441-e1460.

Number of natural disasters worldwide

Number

■ Geophysical events (Earthquake, tsunami, volcanic eruption)	■ Meteorological events (Storm)
■ Hydrological events (Flood, mass movement)	■ Climatological events (Extreme temperature, drought, forest fire)

Prevalence of PTSD since September 11

1.1%	
4.6%	
5.3%	
7.7%	
8.5%	

60   0   60   Miles

22

Distribution of total number of COVOD-19 stressors by post-traumatic stress symptom status
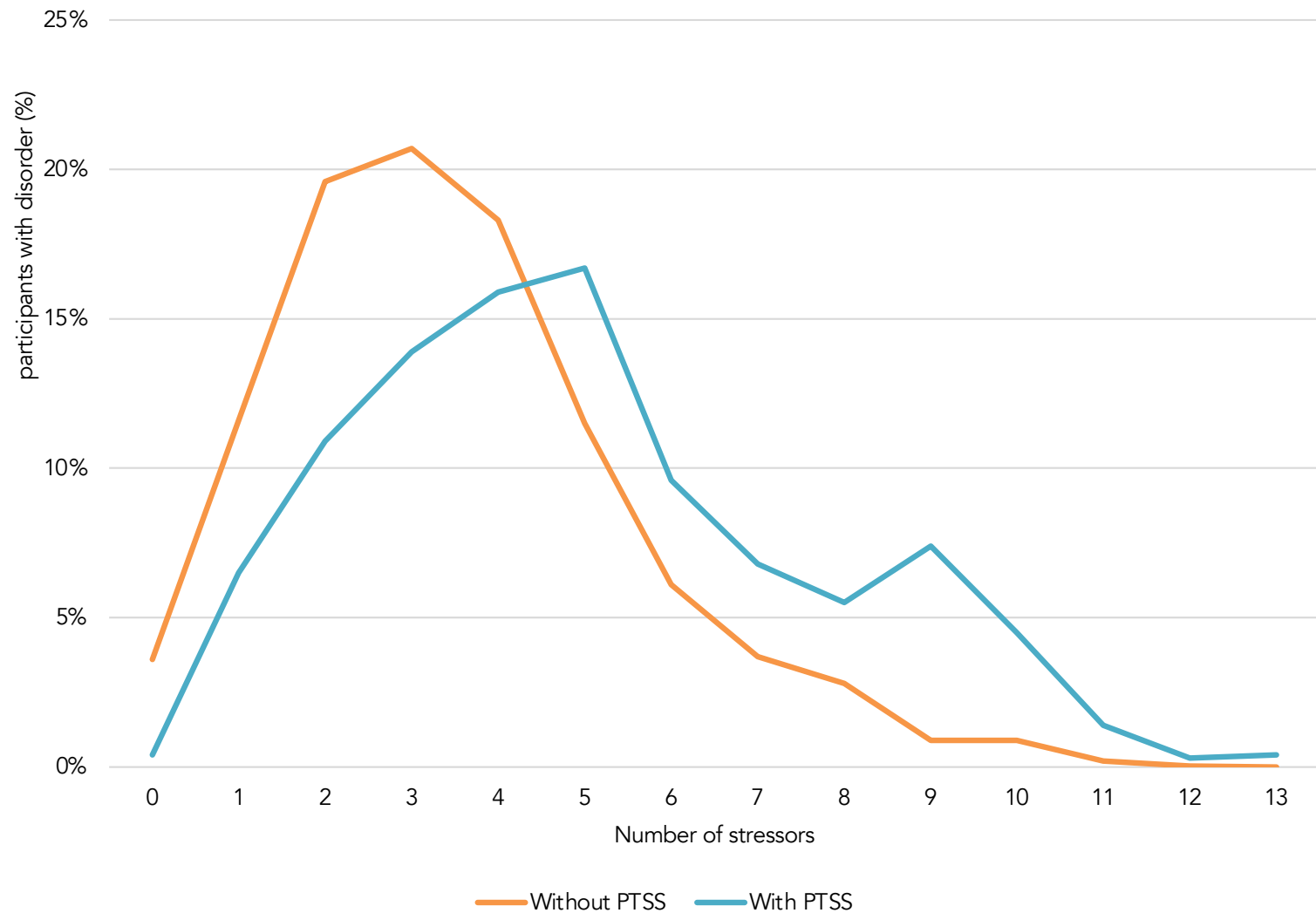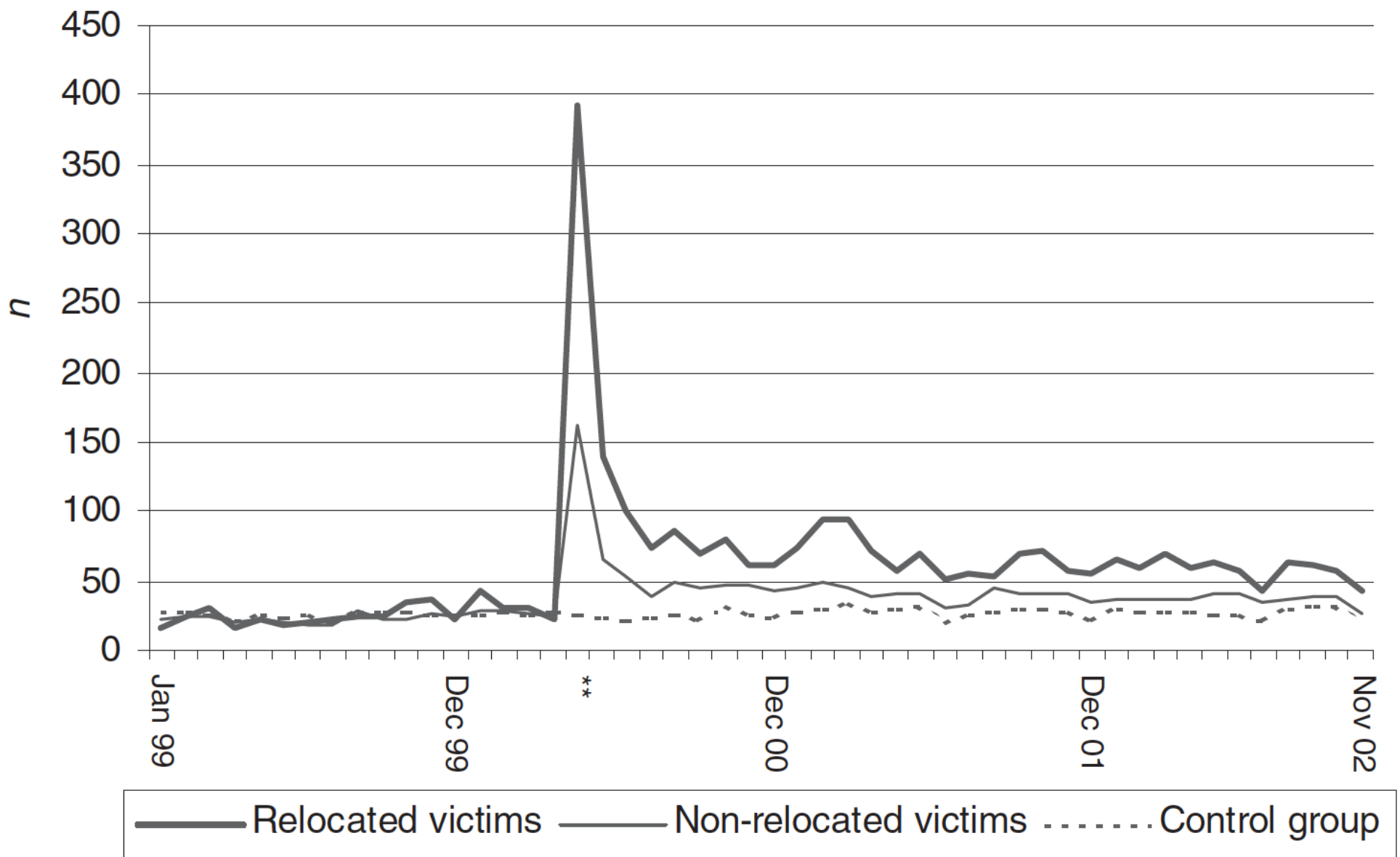
Depression symptoms in U.S. adults before and during the COVID-19 pandemic

3-fold increase

Legend: Before COVID-19: NHANES 2017-2018 | During COVID-19: CLIMB 2020

X-axis categories: None, Mild, Moderate, Moderately severe, Severe

Relocated victims ——— **Non-relocated victims** ······· **Control group**

**Date of disaster.

Yzermans CJ, Donker GA, Kerssens JJ, Dirkzwager AJ, Soeteman RJ, ten Veen PM. Health problems of victims before and after a disaster: a longitudinal study in general practice. Int J Epidemiol. 2005 Aug;34(4):820-6. doi: 10.1093/ije/dyi096. Epub 2005 Apr 28

3. Environmental form
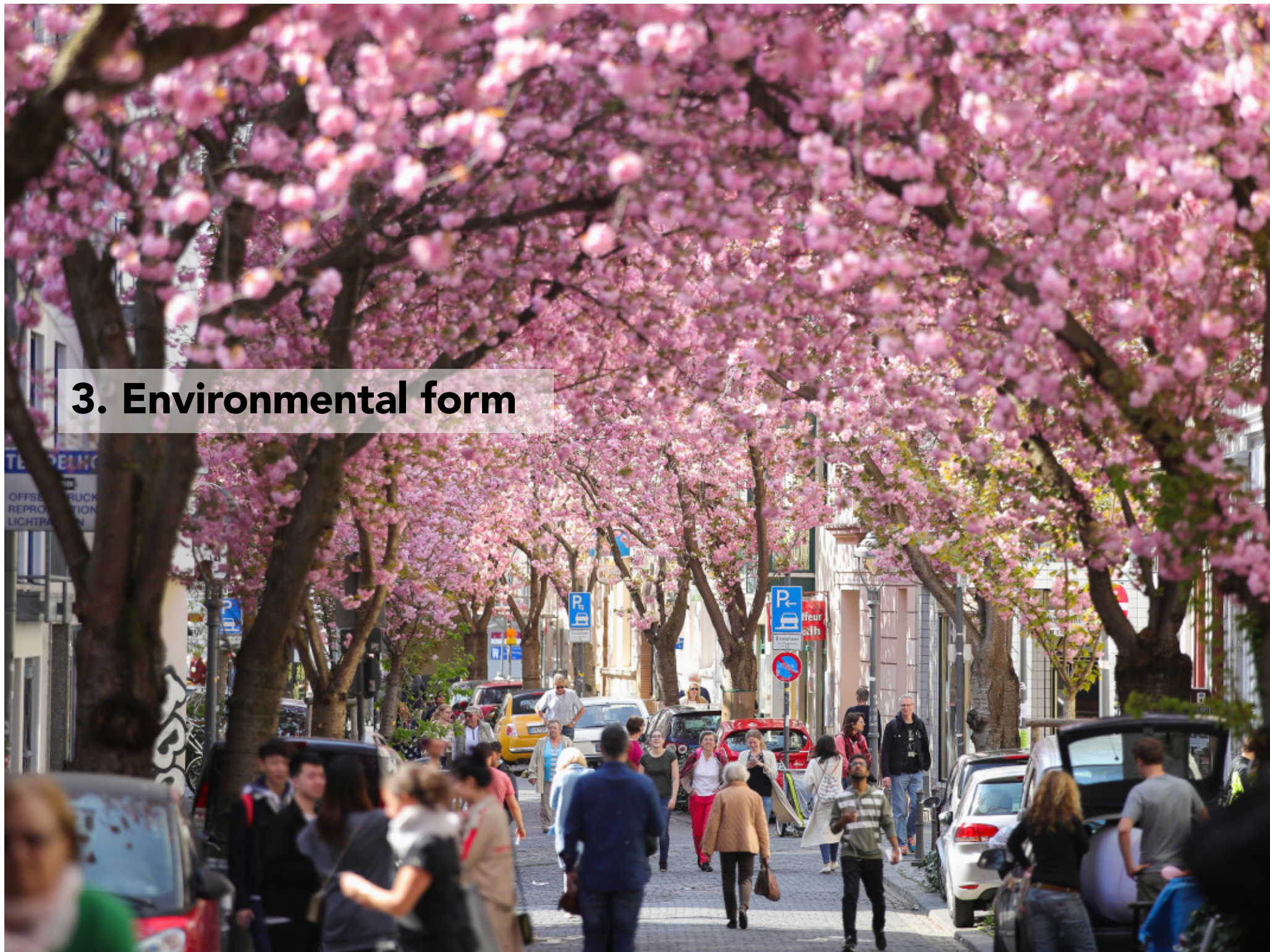
Figure. Associations Between Types of Green Space and Psychological Distress, Depression or Anxiety, and Fair to Poor General Health

A 10-Item Kessler 10 Psychological Distress Scale

B Self-reported physician-diagnosed depression or anxiety

C Self-rated fair to poor general health

Fig. 1. Detroit home owners loan corporation redlining map, 1939.
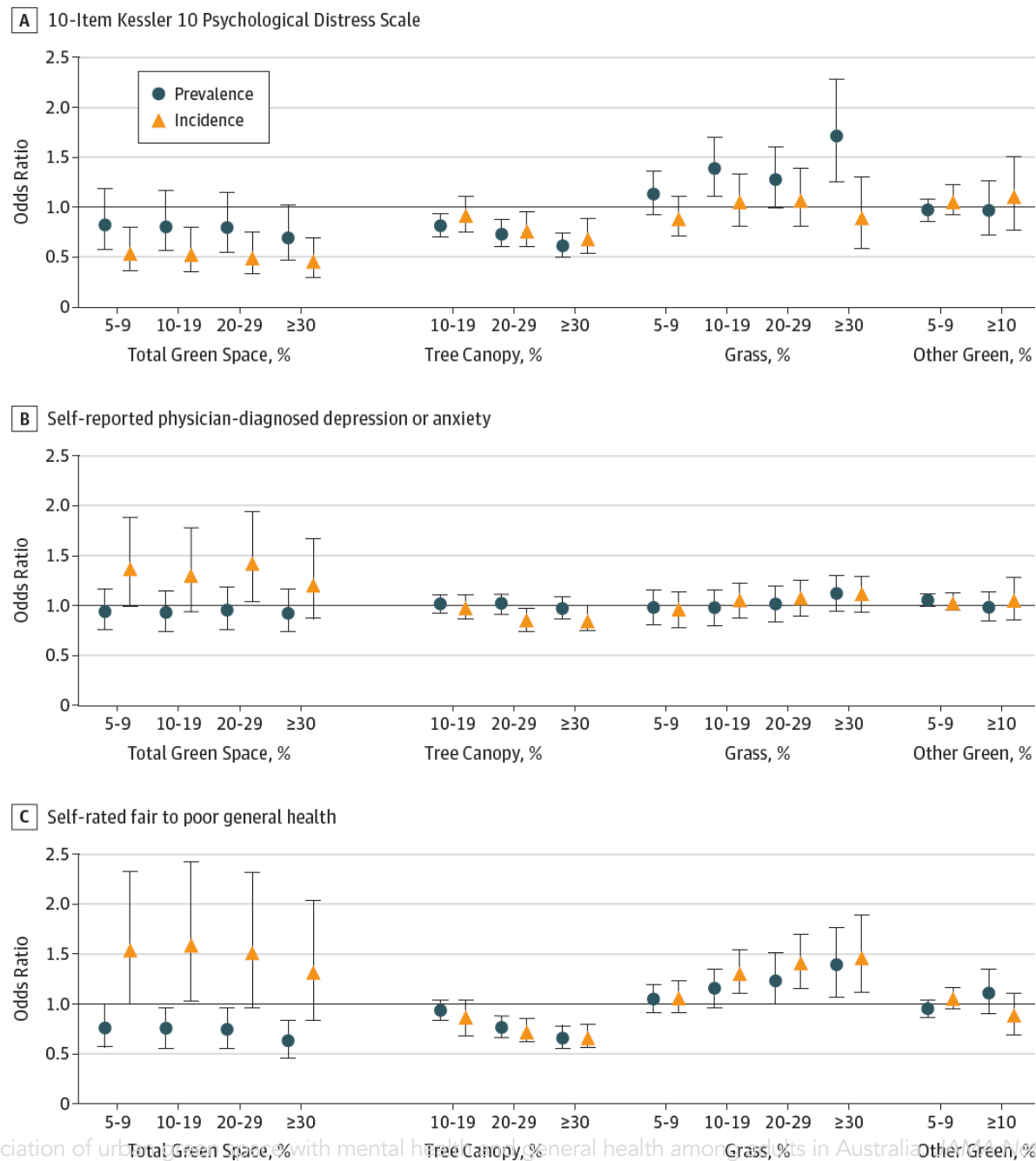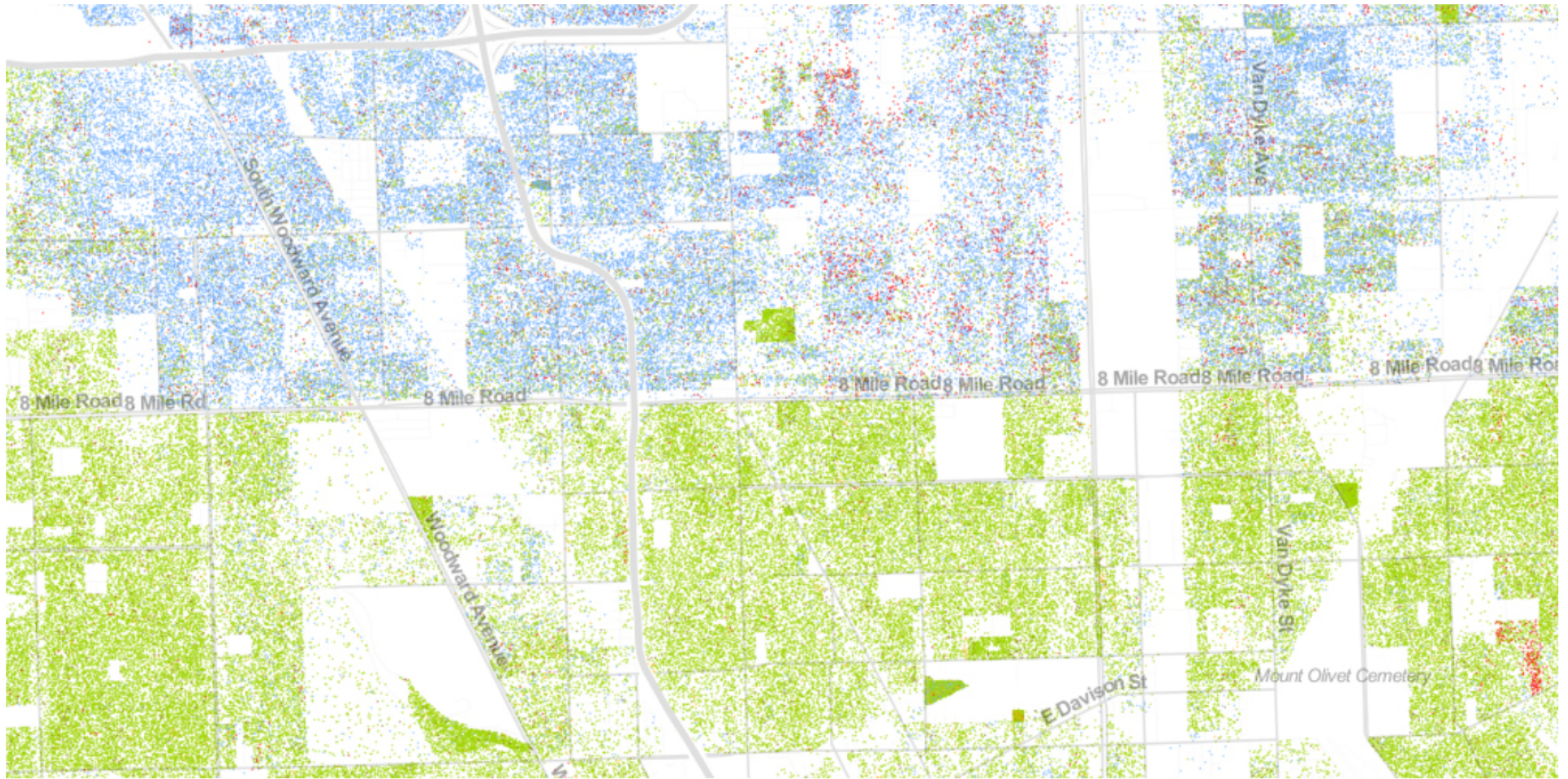
In Detroit, amongst the most segregated cities in America, 8 Mile Road serves as a sharp racial dividing line.
Image: Dustin Cable

http://www.wired.com/2013/08/how-segregated-is-your-city-this-eye-opening-map-shows-you/
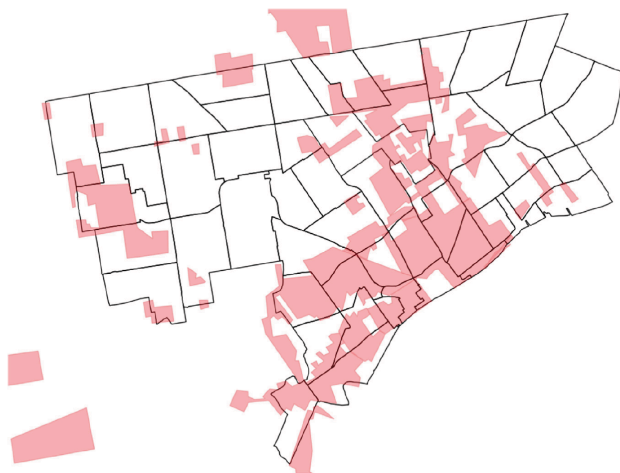
Fig. 3. Redlined areas in city of Detroit planning and development department historic neighborhood
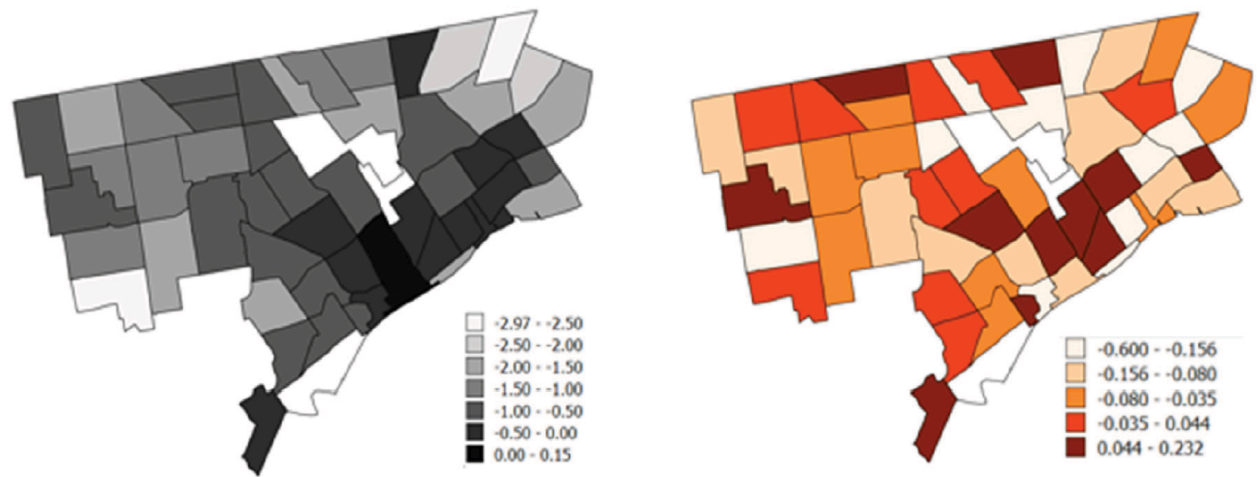
Fig. 4. A. Change in Neighborhood Foreclosure Rate 2009– 2011; Fig. 4B. Change in Prevalence of Poor Self-rated Health 2008–2012.

Foreclosure Rate legend:
- -2.97 - -2.50
- -2.50 - -2.00
- -2.00 - -1.50
- -1.50 - -1.00
- -1.00 - -0.50
- -0.50 - 0.00
- 0.00 - 0.15

Self-rated Health legend:
- -0.600 - -0.156
- -0.156 - -0.080
- -0.080 - -0.035
- -0.035 - 0.044
- 0.044 - 0.232

McClure E, Feinstein L, Cordoba E, Douglas C, Emch M, Robinson W, Galea S, Aiello AE. The legacy of redlining in the effect of foreclosures on Detroit residents' self-rated health. Health and Place. 2019;55:9-19. PMID: 30448354. https://doi.org/10.1016/j.healthplace.2018.10.004

Two key considerations

Equity

Arno, P.S., et al., *Bringing health and social policy together: The case of the earned income Incentive credit.* Journal of public health policy, 2009. **30**(2): p. 198-207.

ALL ADULTS
BY WEALTH RANGE

TOTAL WEALTH
USD

$1M+   0.7%

$100K–1M   7.9%

$10K–100K   21.3%

<$10K

70.1%
of the world's
people are in
the sub-$10K
wealth range

$128.7T   45.9%

0.7%
of the world's
people control
$128.7 trillion
of wealth

$111.4T   39.7%

$32.5T   11.6%

$7.6T   2.7%

Source: Credit Suisse, Forbes

https://www.visualcapitalist.com/global-wealth-concentration/
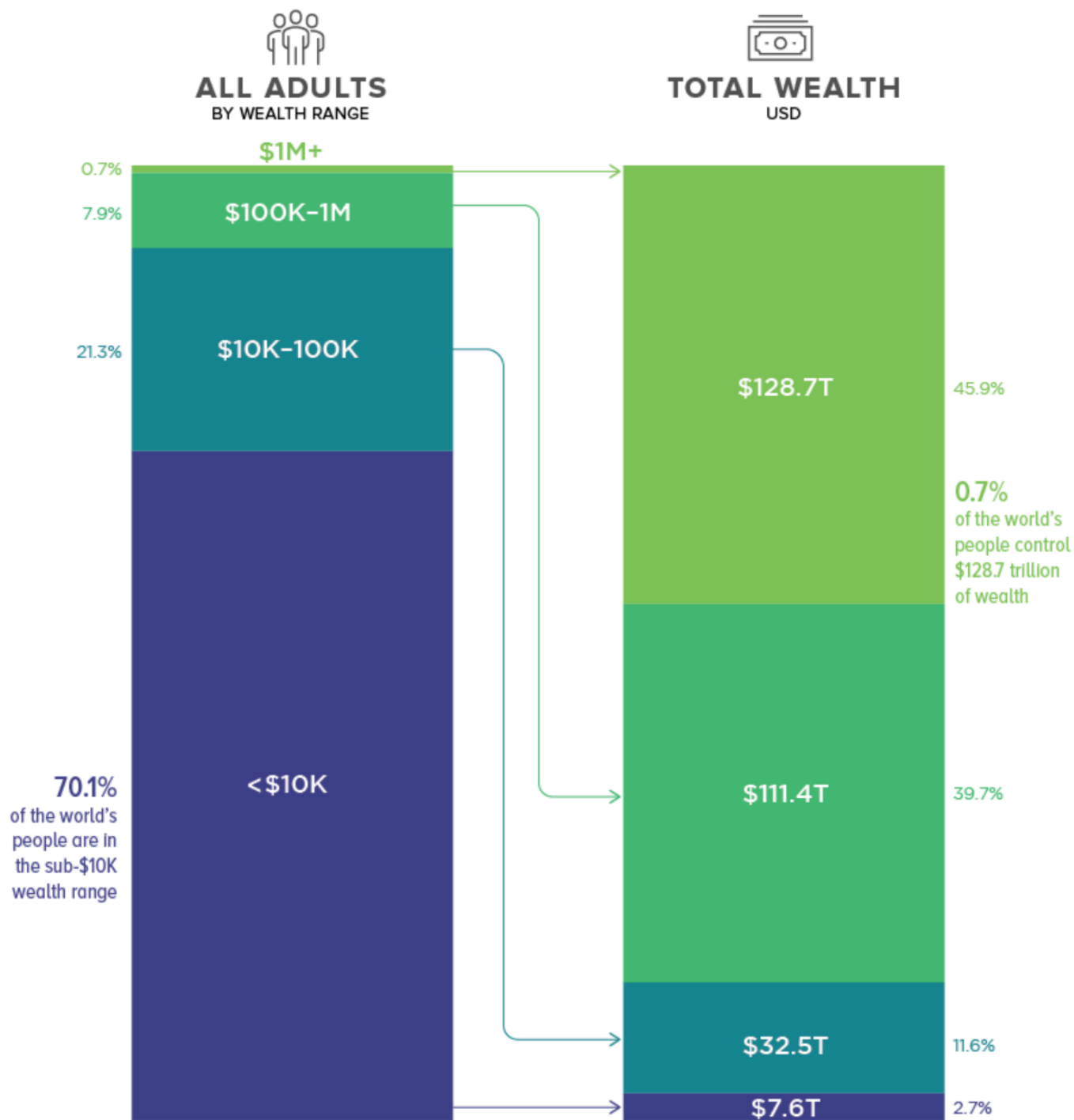
Assets, stressors, and depression during COVID-19
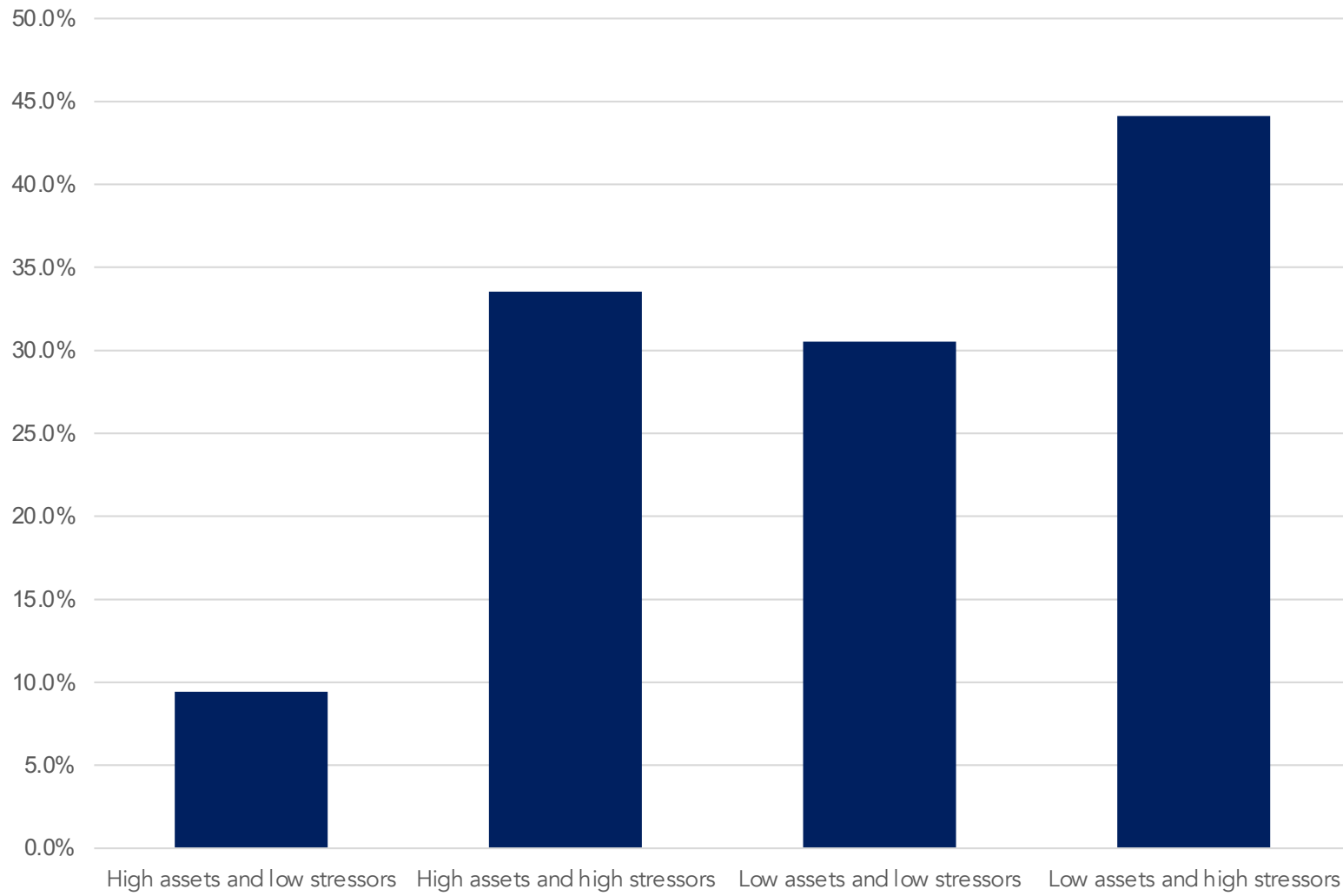
Prevalence of probable depression across different stressors among people with high and low assets, Hong Kong

Probable depression

Wai Kai Hou et al. Civil unrest, COVID-19 stressors, anxiety, and depression in the acute phase of the pandemic: A population-based study in Hong Kong. SPPE. In press.
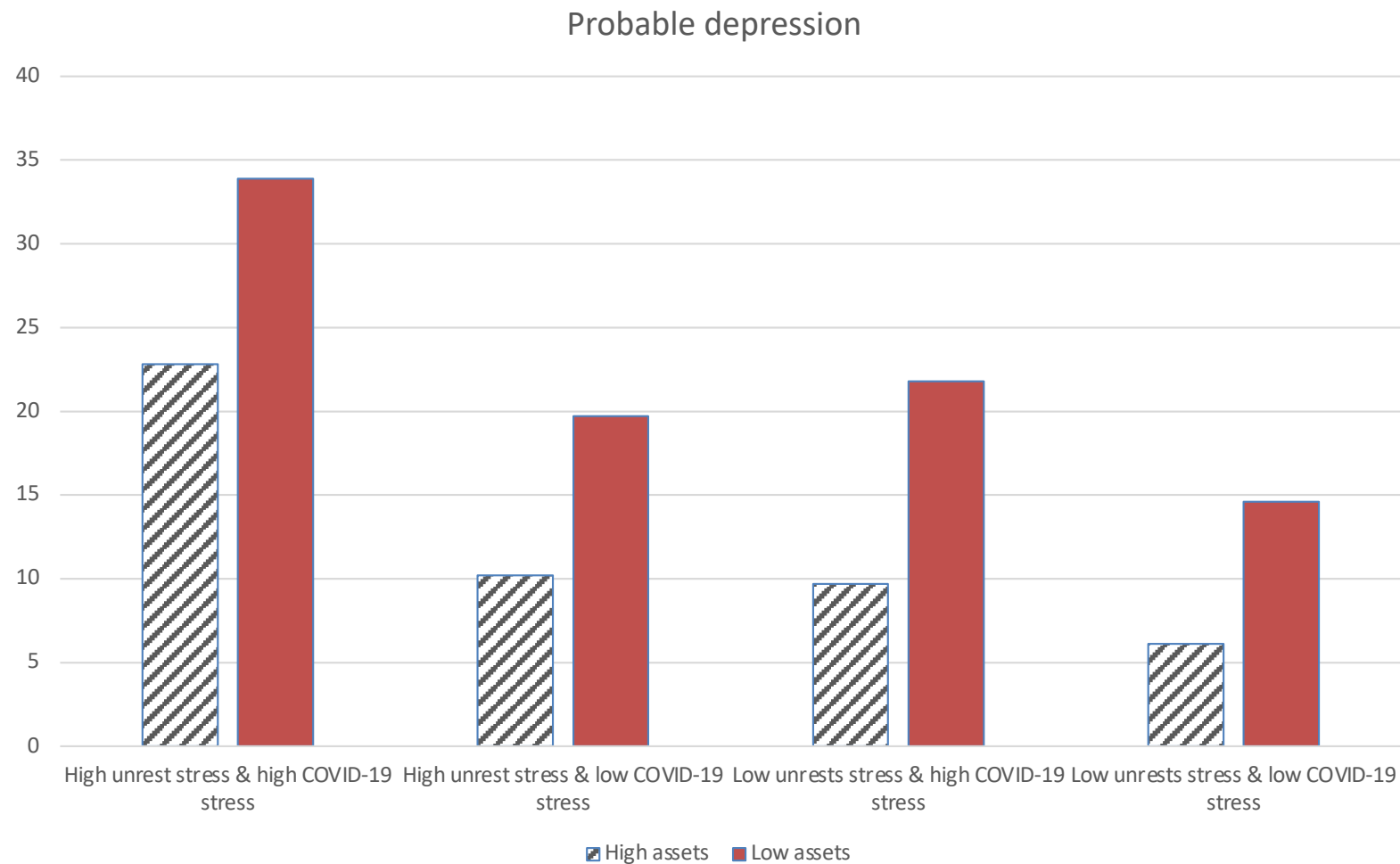
In **the United States**, as of October 22 2020, employment rates among workers in the bottom wage quartile decreased by **21%** compared to January 2020 (not seasonally adjusted).

Oct 22, 2020

+1.6%
High Wage
(>$60K)

-4.4%
Middle Wage
($27K-$60K)

-21%
Low Wage
(<$27K)

+10%
0%
-10%
-20%
-30%

Jan 15
2020

Apr 1

Jun 1

Aug 1

Oct 1

Dec 1

Jan 28
2021

Jan 20
First U.S. COVID-19 Case

Mar 27
CARES Act Enacted

Jan 04
Second Stimulus
Payments Start

Mar 13
National Emergency
Declared

Apr 15
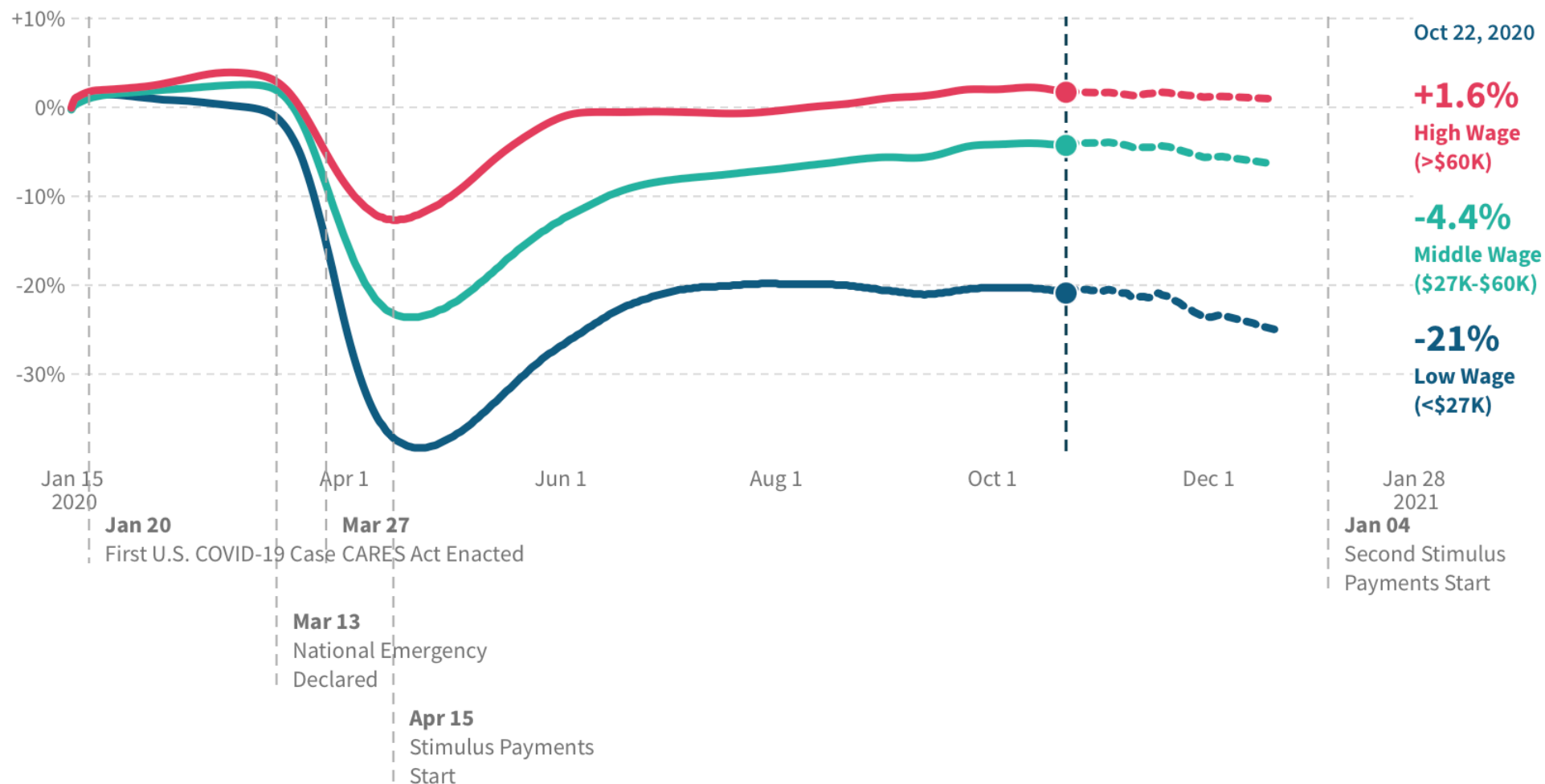Stimulus Payments
Start

https://tracktherecovery.org

Black workers are far more likely to be unemployed than white workers at every level of education

Unemployment rates by race and education, 2019

	Black	White
Overall	6.1%	3.0%
Less than high school	14.7%	8.3%
High school	8.3%	3.9%
Some college	4.9%	2.9%
Bachelor's degree	3.4%	2.2%
Advanced degree	2.3%	1.7%

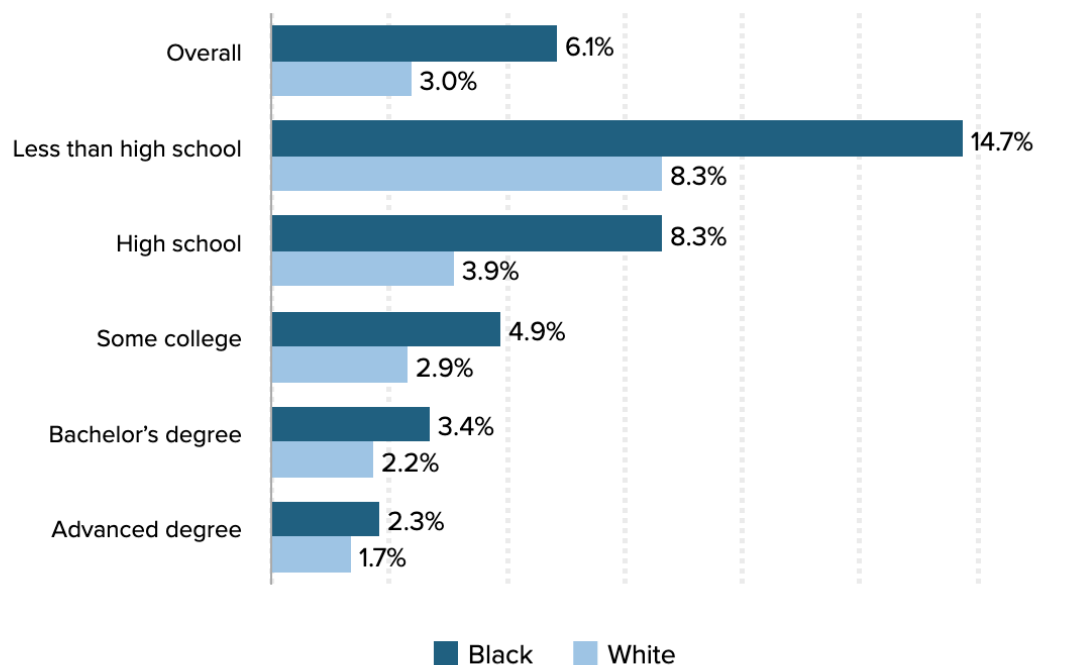■ Black   ■ White

Chart Data

Notes: White refers to non-Hispanic whites, black refers to blacks alone. Educational categories are mutually exclusive and represent the highest education level attained for all individuals ages 16 and older.

Source: Economic Policy Institute, *State of Working America Data Library*, [Unemployment by race and education], 2019.

Economic Policy Institute

Covid-19 stressors and suicidal ideation

Raifman J, Ettman CK, Dean L, Barry C, Galea S. Stressors and suicidal ideation during the COVID-19 pandemic. Under review.
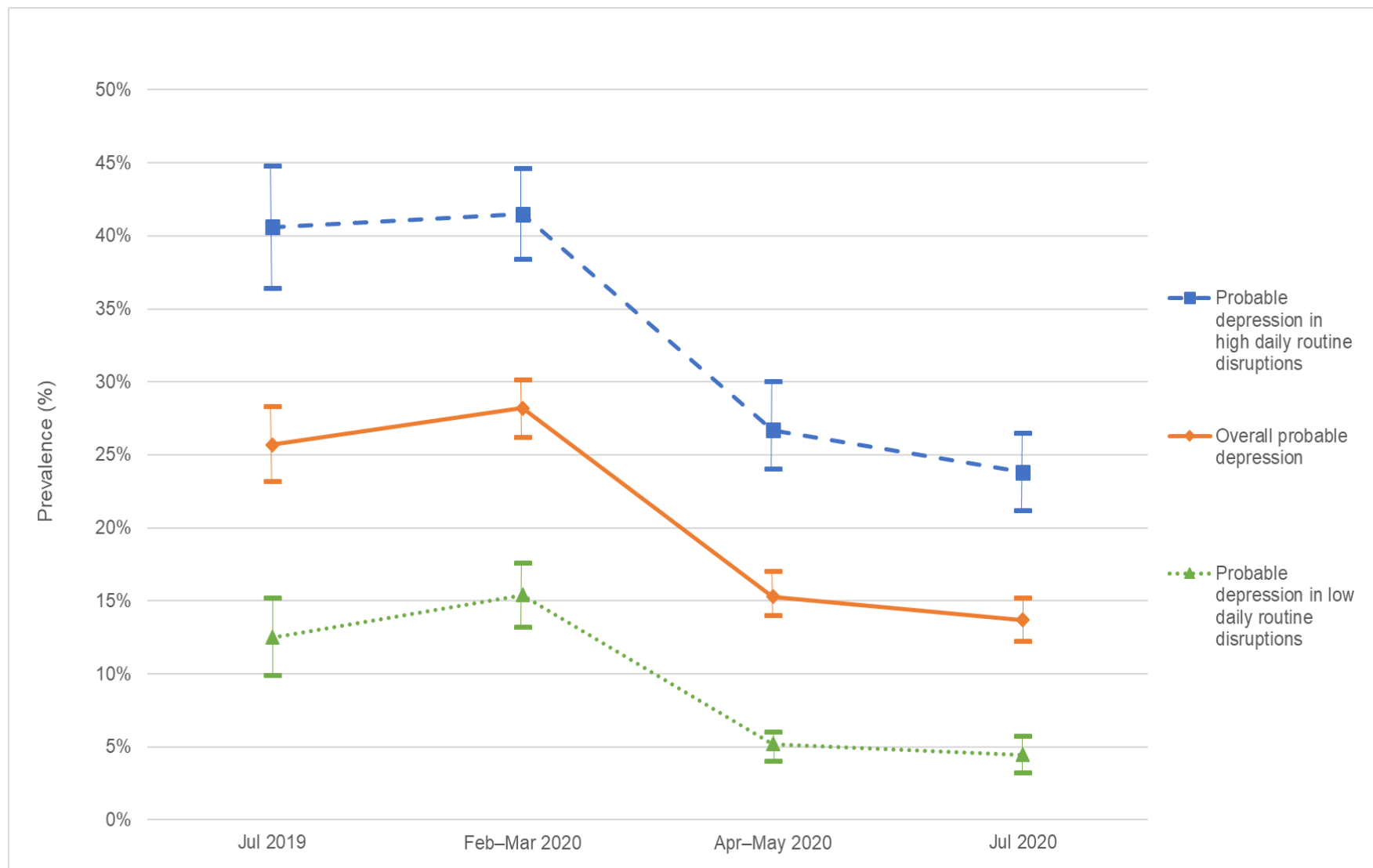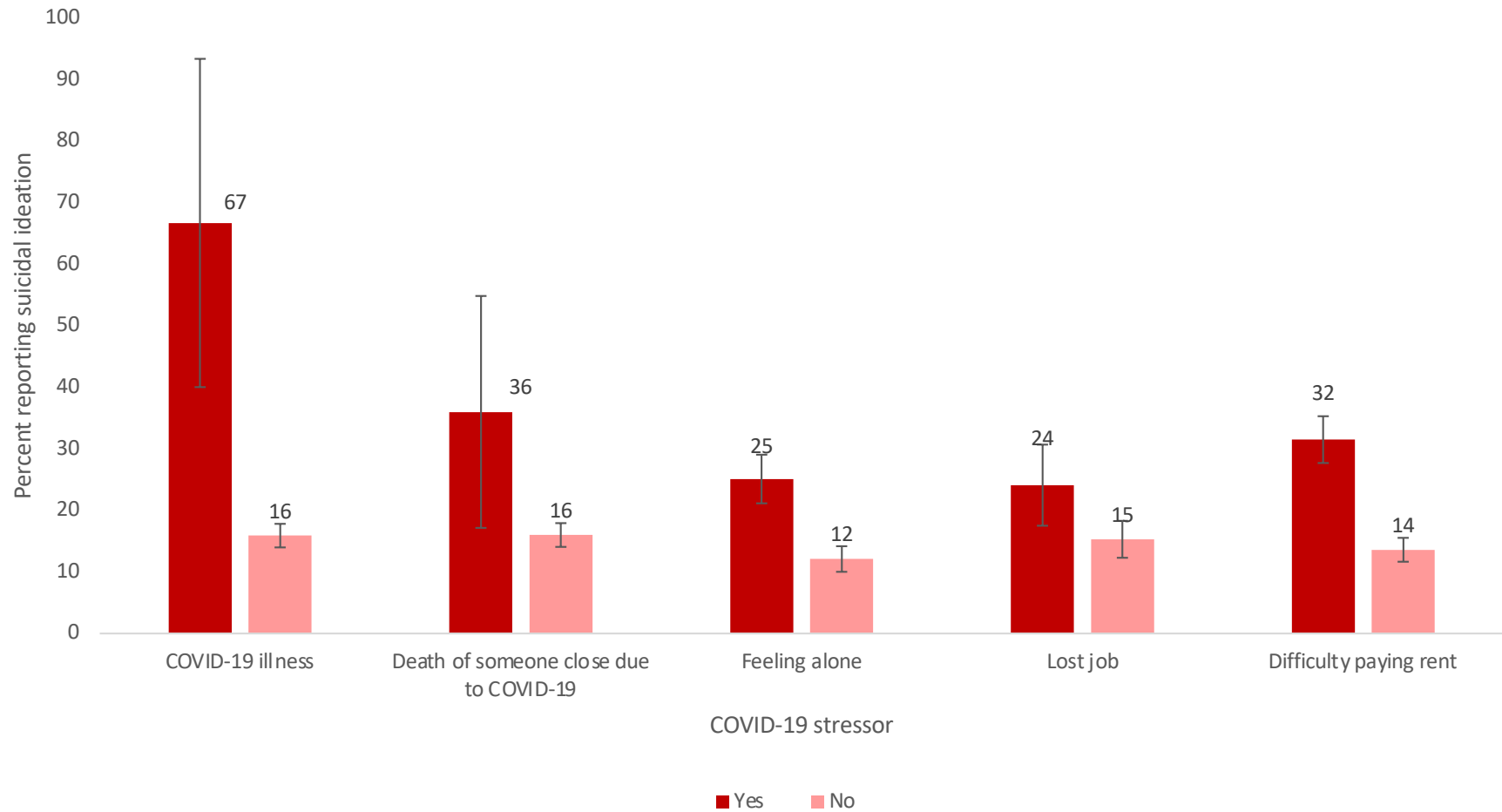
Methods
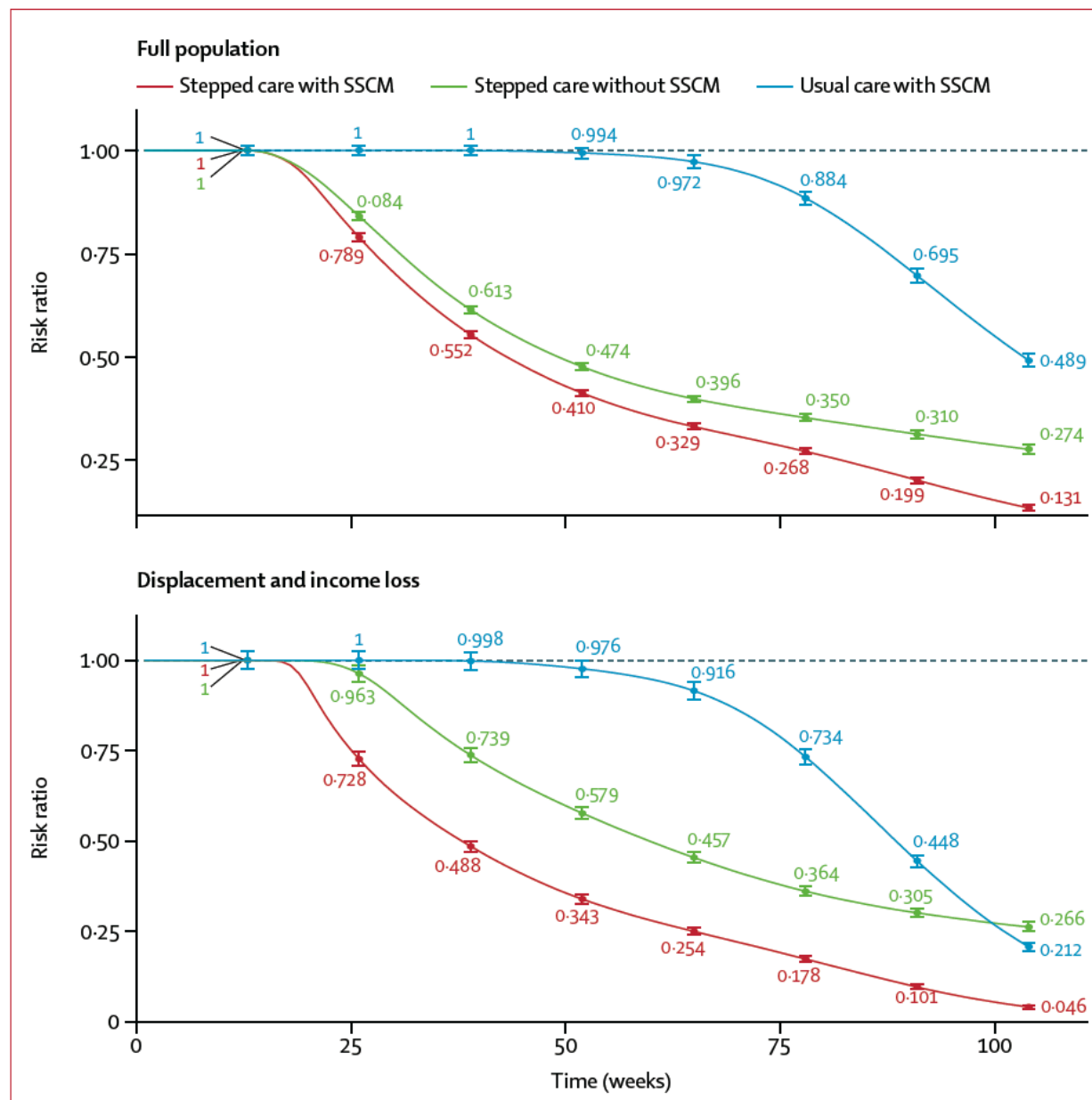
Figure 4: Risk ratios for prevalence and persistence of post-traumatic stress disorder among the full population and agents with displacement and income loss
SSCM=social services case management.

Social and Economic Policies

Institutions

Neighborhoods and Communities

Living Conditions

Social Relationships

Individual Risk Factors

Genetic/Constitutional Factors

Pathophysiologic pathways

Individual/Population Health

Lifecourse

Environment

Kaplan, G. What's wrong with social epidemiology, and how can we make it better? *Epid Rev* 2004; 26: 124-135

Family-level/psychosocial exposures						Area-level/structural exposures	
Family poverty	Residential mobility	Neighborhood social cohesion	Neighborhood disorder	Neighborhood crime	Neighborhood deprivation	Air pollution	Urbanicity
Parent interviews	Participant and parent interviews	Resident surveys	Resident surveys	Police data	Consumer classifications	Air-quality models	Census data
Birth to age 5	Birth to ages 12/18	Age 12	Age 12	Age 18	Ages 5/12/18	Ages 10/18	Ages 5/12/18

Newbury JB et al. Association between genetic and socioenvironmental risk for schizophrenia during upbringing in a UK longitudinal cohort. 2020; Psychological Medicine 1–11. https://doi.org/ 10.1017/S0033291720003347

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