Despair and Aging in Southern Appalachia: The Great Smoky Mountains Study

William E. Copeland PhD

INRPHA webinar

February 13th 2026

Duke

Disclosures

I have received grant support from NIMH, NICHD, NIA, NIDA, and the Brain and Behavior Research Foundation

I receive funding from the nonprofit Research Center for Children, Youth and Families which publishes commonly-used questionnaires (e.g., CBCL, YSR, TRF)

Structure of talk

The history of GSMS

GSMS-RA

A little data on despair and aging

Life in 1993 . . .

The World

- End of Cold War era; Berlin wall was down
- European Union officially formed

Tech

- Windows 3.1 and early home PCs
- Dial-up Internet emerging (e.g., AOL)
- CD players and VHS common

Pop Culture

- Music: Nirvana, Whitney Houston, Dr. Dre
- Movies: Jurassic Park, The Fugitive
- TV: Friends and The X-Files debuted

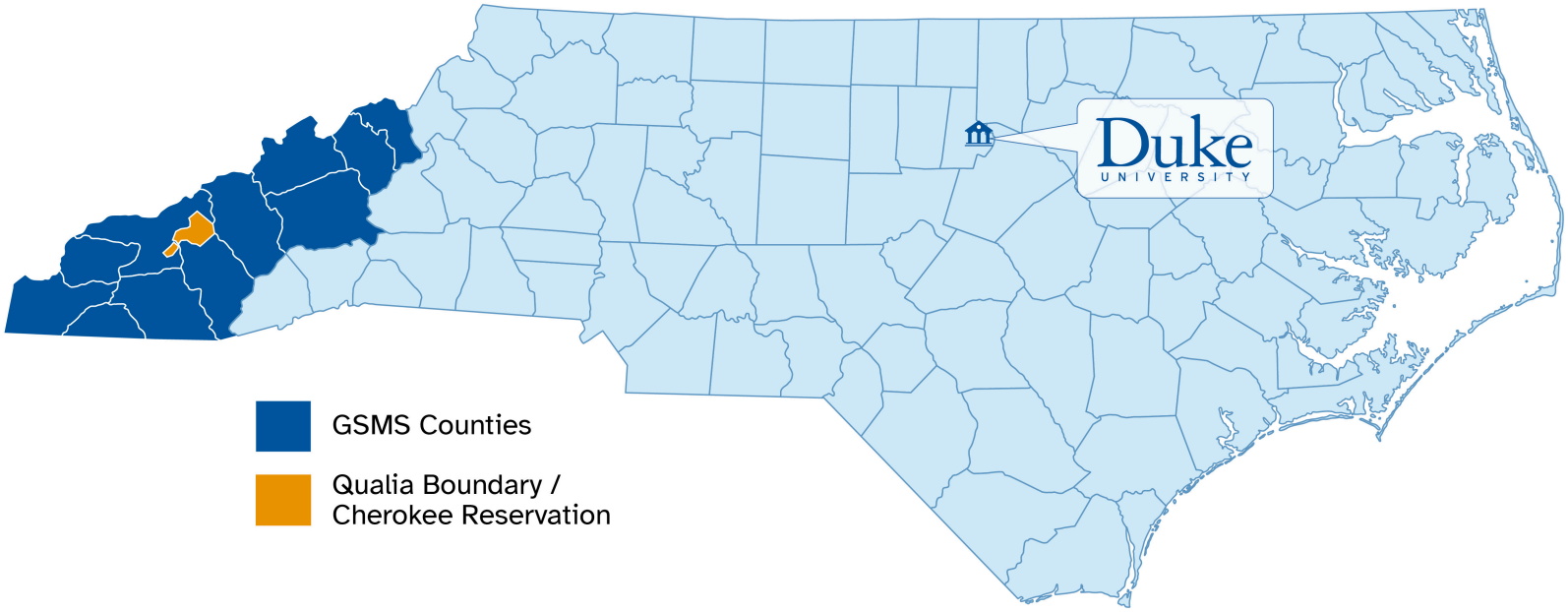
Everyday life

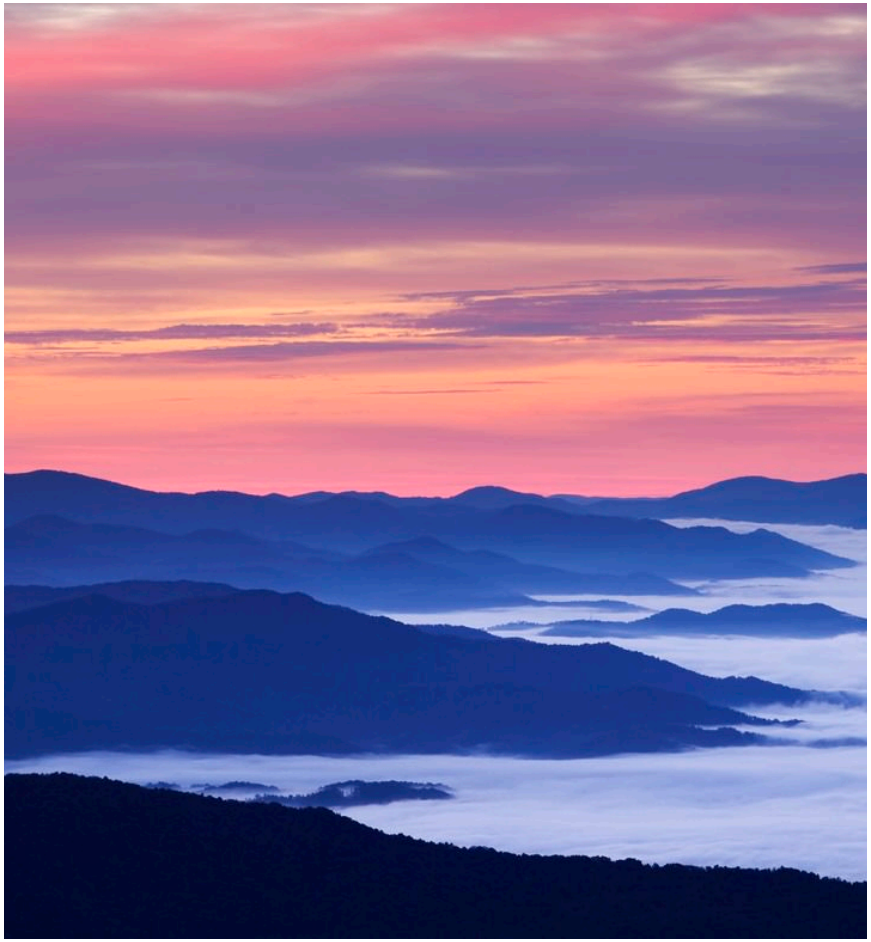
- No smartphones or streaming
- Malls and video rentals were social hubs
- Baggy jeans, flannel, neon fashion

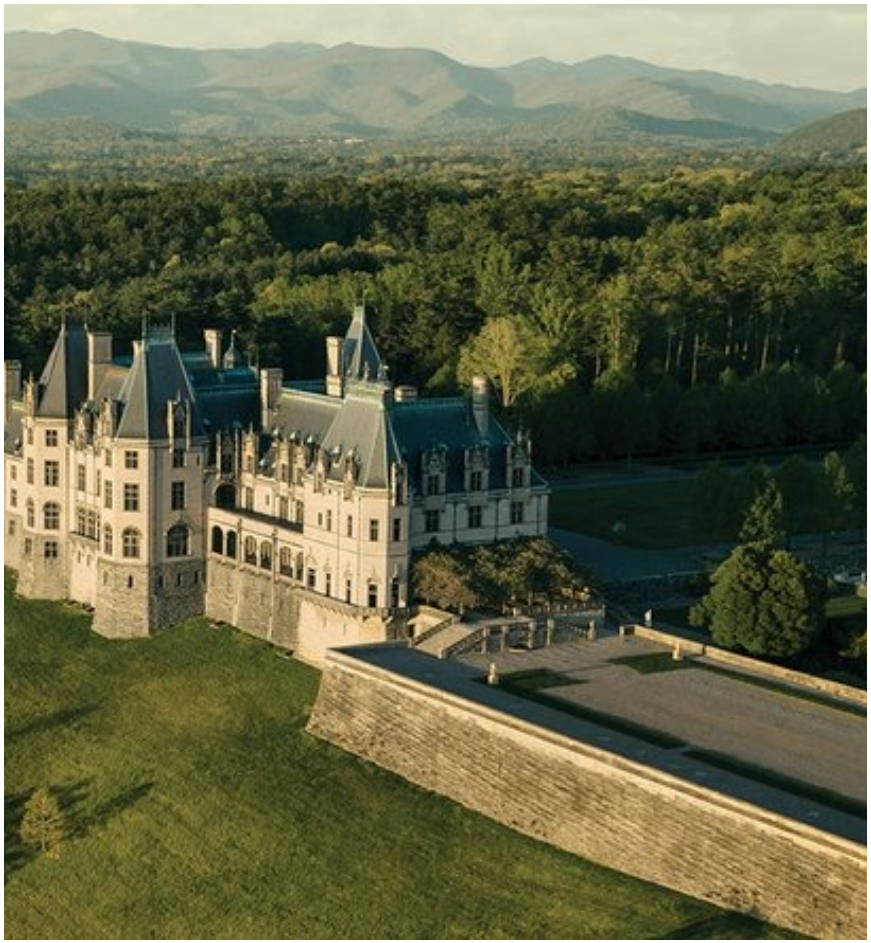
"The Great Smoky Mountains Study (GSMS) was designed to examine the development of, need for, and use of mental health services in children and adolescents in an area of the southeastern United States."

Map of GSMS Study Area

Counties include: Buncombe, Clay, Cherokee, Graham, Haywood, Jackson, Macon, Madison, Mitchell, Swain, and Yancy








WELCOME
CHEROKEE INDIAN
RESERVATION

The Great Smoky Mountains Study

- Study began in 1993
  - N_{total}= 1420 (9-13 years)
  - N= 350 Eastern Band of Cherokee Indian children
- Community-representative, prospective, longitudinal
- Longitudinal follow-up over 30+ years
  - Childhood (ages 9-12)
  - Adolescence (ages 13-16)
  - Young Adulthood (ages 19, 21)
  - Adulthood (ages 25, 30, late 30s, and early 40s)

History of the Study

FIRST FUNDED BY NIMH IN 1992

SUPPORT SHIFTED TO NIDA IN 1997 TO UNDERSTAND SUBSTANCE USE PATTERNS IN TEENS AND TWENTIES

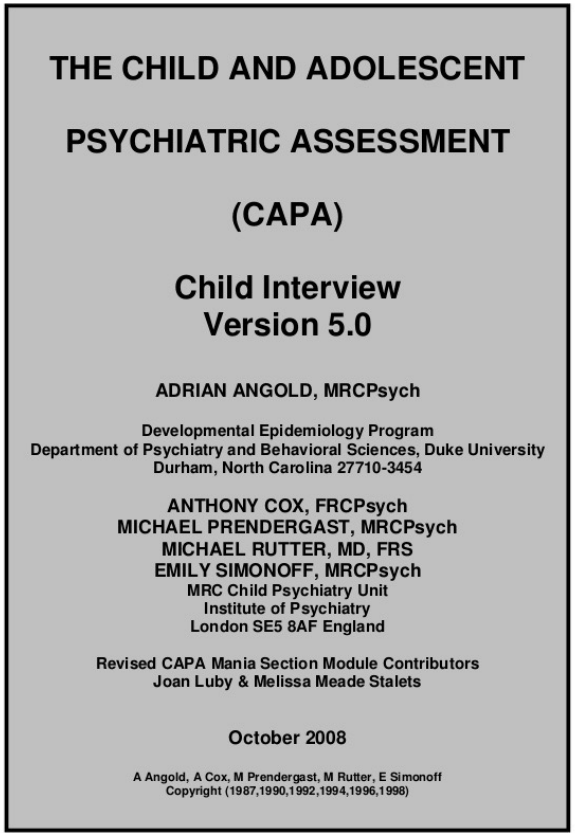
LATER FUNDED BY NICHD TO STUDY INTERGENERATIONAL TRANSMISSION OF RISK AND RESILIENCE

MOST RECENTLY FUNDED BY NIA TO STUDY AGING IN A RURAL CONTEXT

1993 2000 2005 2010 2015 2020 2023

9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37		39	40	41	42	43
11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	44
13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47

Cohort ages



THE CHILD AND ADOLESCENT

PSYCHIATRIC ASSESSMENT

(CAPA)

Child Interview
Version 5.0

ADRIAN ANGOLD, MRCPsych

Developmental Epidemiology Program
Department of Psychiatry and Behavioral Sciences, Duke University
Durham, North Carolina 27710-3454

ANTHONY COX, FRCPsych
MICHAEL PRENDERGAST, MRCPsych
MICHAEL RUTTER, MD, FRS
EMILY SIMONOFF, MRCPsych
MRC Child Psychiatry Unit
Institute of Psychiatry
London SE5 8AF England

Revised CAPA Mania Section Module Contributors
Joan Luby & Melissa Meade Stalets

October 2008

Assessment

- Structured diagnostic interview of participants and their parents
  - Child and Adolescent: CAPA (ages 9-16)
  - Young Adult: YAPA (ages 19+)
- Structure diagnostic interview of parent's MH
- Biomeasures at each assessment
  - Height, weight, pulmonary function
  - Blood spot collection of 10 spots (7000+ banked dried bloodspots)
- Linkage to education, criminal, juvenile justice, voting, and health records
- Geospatial coding and census data linkage

Data Collection across GSMS Waves

Individual
- History of physical development; BMI
- History of illness and disability
- Health risk behaviors, HIV and AIDS risk

Pubertal development; early puberty

Peer and other social relations

Relations in school or work
- Relations out of school or work
- Gang membership
- Deviant peer group
- Leadership, rejection, neglect
- Sexual relationships, marriage, parenting

Relations with other adults
- Relations with teachers

Relations with employers

Relations with other adults

School functioning
- School work, attainment

Higher education, work, income
- Age at school leaving, graduation
- Higher education
- Work history
- Income, income/need ratio

Experience of trauma and violence

Physical abuse and neglect
- Sexual abuse

Other traumatic events
- Delinquency and crime
- Self and parent reports of offending
- Juvenile court records
- Adult criminal records

Other
- Guns in home
- Other life events
- Spirituality and religious faith
- Need for MH care
- Use of services for MH problems

Family

Family of origin
- Number and age of other children in home
- Stability of family structure
- Teenage parents

Family of residence
- Marital history
- Number and ages of children
- Stability of family structure

Family relations
- S's relations with parental figures
- S's relations with siblings
- Relationship of parenting figures to S

Relations between parenting figures

Relations with spouse and children

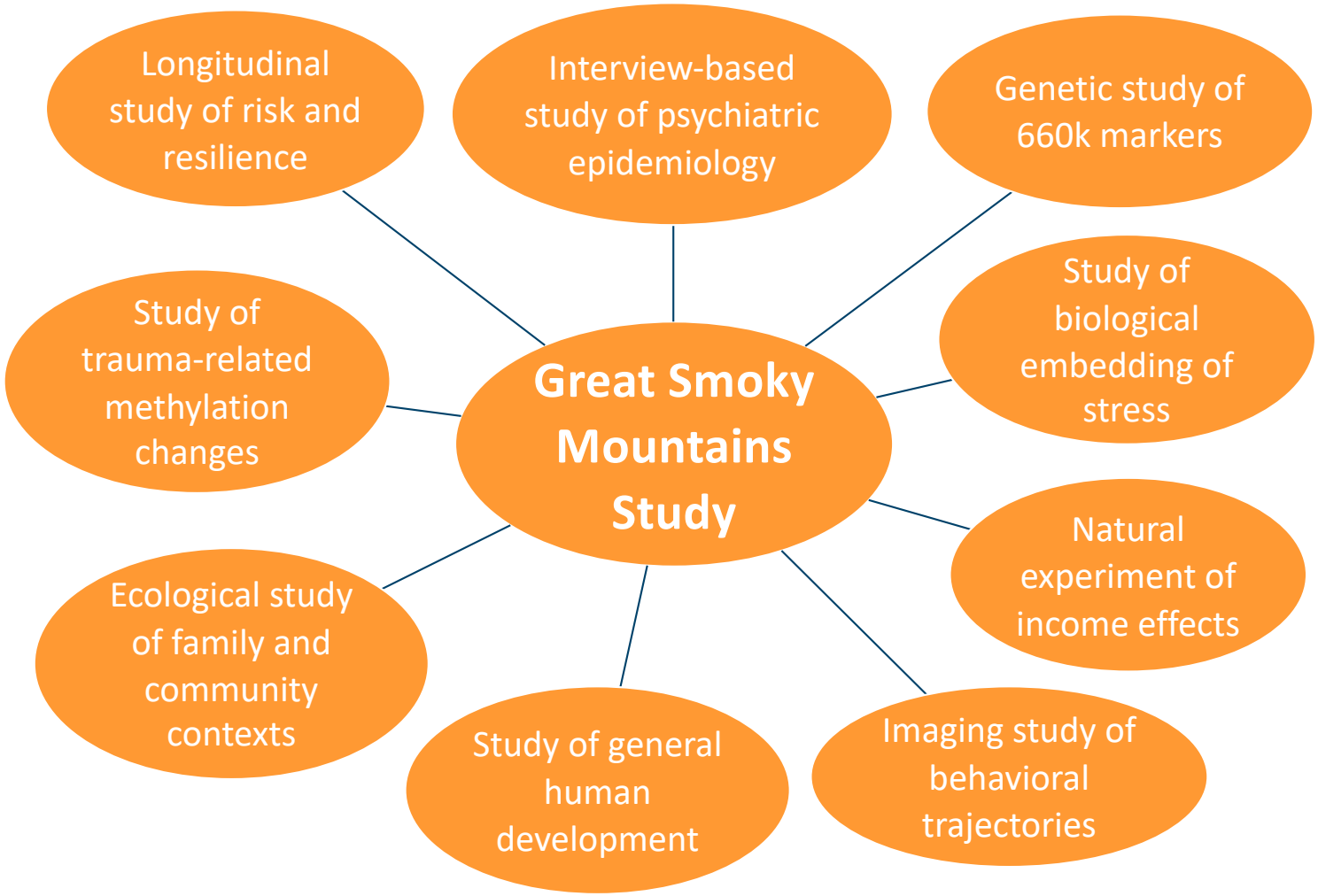
Family resources
- Income, sources, and stability
- Income, sources, and stability
- Amount of education
- Employment and unemployment
- Health and insurance
- Access and barriers to care
- Family burden

Psychiatric and criminal history
- Family history of arrest for crime
- Family history of drug problems
- Family history of psychiatric disorder
- Family history of suicide
- Current maternal depression

Other characteristics of family of origin
- Guns in the home
- Spirituality and religious faith
- Attitudes and barriers to use of MH services

School and post-school educational settings
- Per-student expenditure
- Ranking on standardized tests
- Official reports of violence
- S's perception of violence

Community characteristics
- Number and training of professionals
- S's perception of neighborhood
- Neighborhood crime: Census and FBI data


Great Smoky Mountains Study
Longitudinal study of risk and resilience
Interview-based study of psychiatric epidemiology
Genetic study of 660k markers
Study of trauma-related methylation changes
Study of biological embedding of stress
Natural experiment of income effects
Ecological study of family and community contexts
Study of general human development
Imaging study of behavioral trajectories

Scientific Impact

- >150 scientific publications; >20% pubs rated as highly cited (top 1% by citations)

- Psychiatric epidemiology
- MH Service use and unmet need
- Develop of and risk for emotional and behavioral problems
- Childhood exposure to life events including trauma and bullying
- ‘Natural’ Experiment of casino effect
- Puberty and Mental Health
- Substance use risk and trajectories
- Adult outcomes of early experiences
- Despair and its diseases (including opioid use)

What makes Smoky special?

- Representative sampling of a high-risk rural community
- Prospective assessment of early life
- In-depth focus on mental health and psychosocial risk
- Long-term follow up into adulthood
- Low attrition across 3+ decades
- Serial biosamples across entire study period
- Linkages to administrative data sources (e.g., Census, Education, Criminal Justice)
- Rigorous assessment of cognitive and physical health in adulthood
- Intergenerational assessments of children of participants

Structure of talk

The history of GSMS

GSMS-RA

A little data on aging and despair

The Great Smoky Mountain Study of Rural Aging (GSMS-RA)

GSMS-RA funded by **National Institute on Aging (NIA)**

PIs: **William Copeland** (U of Vermont); **Kathleen Cagney** (UMichigan); **Joe Hotz** (UChicago) **Kenneth Dodge** (Duke), and **Naomi Duke** (Duke)

Continued focus on: Collecting measures of mental, physical & behavioral health, including substance abuse.

New Study: GSMS of Rural Aging (GSMS-RA)

- **New objectives** in GSMS-RA:
  - Create a resource of the study of health and aging in a rural part of the Southeastern US
  - Characterize everyday life and community context in a rural area
  - “Harmonize” measures (of health, economics, etc.) in GSMS-RA to existing national studies like Add Health, PSID, NLSY, HRS, and other studies.

What did we propose to do?

- Data collection to begin fall 2021 and continue for 4 years
- Complete a full assessment of participants' physical health, mental health, family history, substance use, social, community, and economic functioning in their early 40s.
  - 90-100 minute survey
  - Cognitive measures to assess processing speed, memory, problem-solving
  - Biological measures collection – height, weight, blood pressure, pulmonary function
  - Physical function – balance, gait speed, strength, endurance, grip strength
  - Sensory function
  - Blood for biomarker assaying

What did we propose to do?

- Complete a 6-month assessment of everyday health, economic, emotional, and social functioning
  - Biweekly 10-minute surveys
  - 3-1 week wearables (e.g., fitbit-type) to assess sleep, physical activity
- Create neighborhood/community profiles using block group level census data and surveys of collective efficacy (social cohesion and informal control)
- Harmonize data with other studies to allow cross-study comparisons

GSMS BioBox

- Sent to all participants that we are unable to meet with in person (can be shipped international)
- Contains instructions for self-administration or can be completed with phone of video call
- Provides cognitive, sensory, physical performance assessment as well as collect blood.
- Box includes:
  - A booklet that included instructions for all measures, a record sheet for results to some items as well as paper and pencil cognitive tasks;
  - A Tasso kit for collection of dried bloodspots;
  - measures for sensory assessments (smell pens, taste strips, touch wand, vision chart)
  - tape measure for body measurements;
  - fitness tracker for actigraphy.

Physical Performance

- Balance assessments
- Chair Stands
- Timed walks

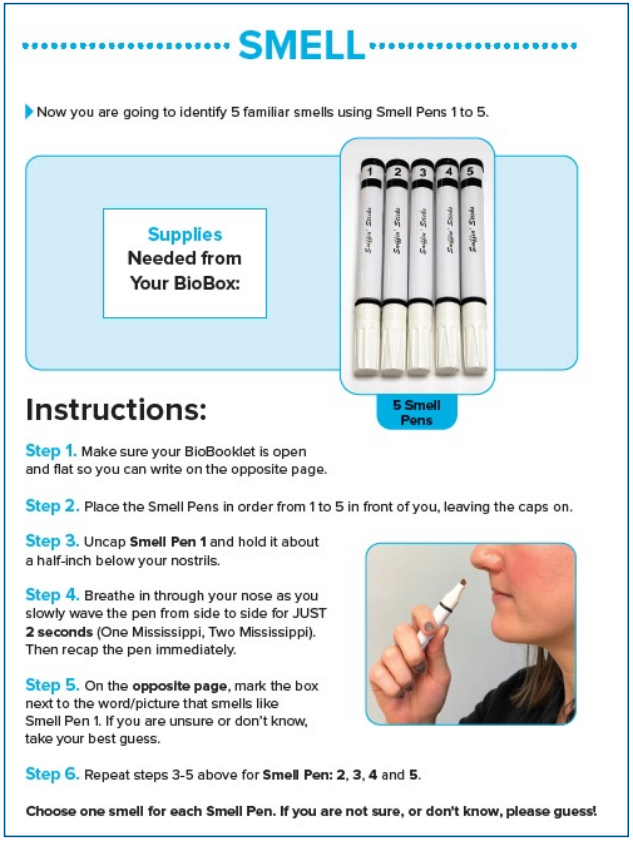
Sensory Function

Touch

Taste

Vision

Smell



SMELL

Now you are going to identify 5 familiar smells using Smell Pens 1 to 5.

Supplies Needed from Your BioBox:

5 Smell Pens

Instructions:

Step 1. Make sure your BioBooklet is open and flat so you can write on the opposite page.

Step 2. Place the Smell Pens in order from 1 to 5 in front of you, leaving the caps on.

Step 3. Uncap **Smell Pen 1** and hold it about a half-inch below your nostrils.

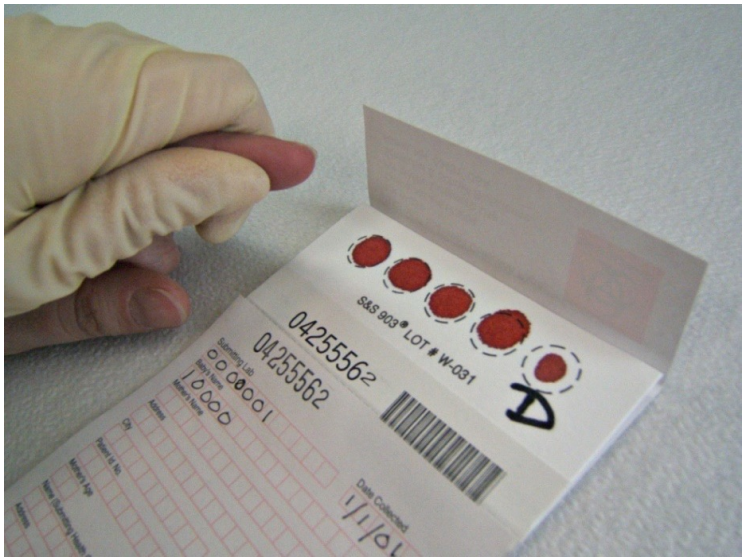
Step 4. Breathe in through your nose as you slowly wave the pen from side to side for JUST **2 seconds** (One Mississippi, Two Mississippi). Then recap the pen immediately.

Step 5. On the **opposite page**, mark the box next to the word/picture that smells like Smell Pen 1. If you are unsure or don't know, take your best guess.

Step 6. Repeat steps 3-5 above for **Smell Pen: 2**, **3**, **4** and **5**.

Choose one smell for each Smell Pen. If you are not sure, or don't know, please guess!

Blood Spots



Bloodspot from lancet

Bloodspot from Self-administered TASSO kit

GSMS-RA: Scorecard

Target	Result	Goal met?
1. Reengage high % of sample	945 of 1330 (71%) living participants consented and completed survey	👍👍👍
2. Collect aging baseline (physical, sensory, cognitive measures)	779 (82%) participants completed full battery of measures	👍👍
3. Collect biosamples	746 (78.9%) participants provided blood samples via dried blood spots or TASSO kit	👍👍
4. Engage remote participants	195 participants completed aging and biosample measures remotely via BioBox	👍👍👍
5. Complete “Everyday Life” assessments	533 completed at least one follow up “Everyday Life survey”. Average number of assessments completed =7.8	👍👍
6. Collect wearable data	Had to be discontinued due to low enrollment	👎
7. Disseminate to other researchers	Data processing and codebook creation are still underway.	Incomplete

GSMS and GSMS-RA – Test Bed for Survey Innovation

1. We used GSMS-RA subsample to assess GPS tracking with smartphones to extend "activity space" research to rural areas.
2. Using GSMS-RA subsample to test & validate questions for recalling earlier life health events/conditions.
   - Assessing ability of mid-life Rs to accurately recall such events/conditions, using their responses in earlier waves of GSMS.
3. Part of *Collaborative for Innovation in Data & Measurement in Aging* (CIDMA) funded by collaborative Cores in UMichigan (Cagney, PI) and UChicago (Hotz, PI) P30 NIA center grants.

Structure of talk

The history of GSMS

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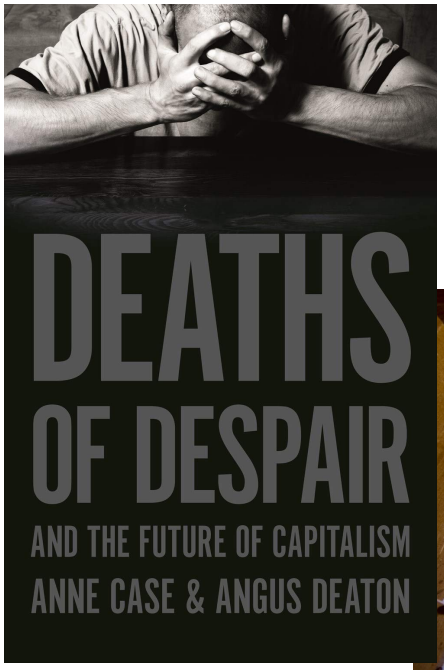
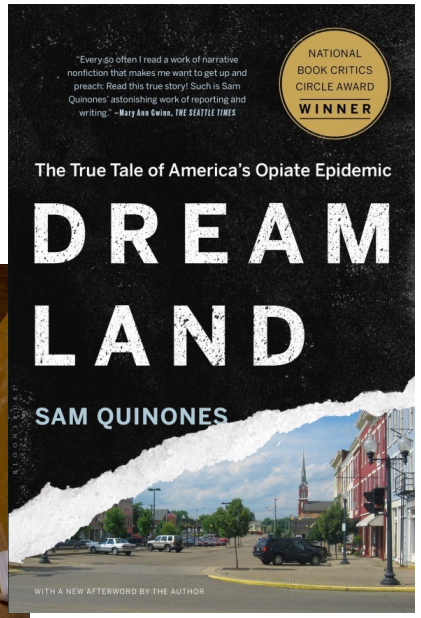
A little data on aging and despair

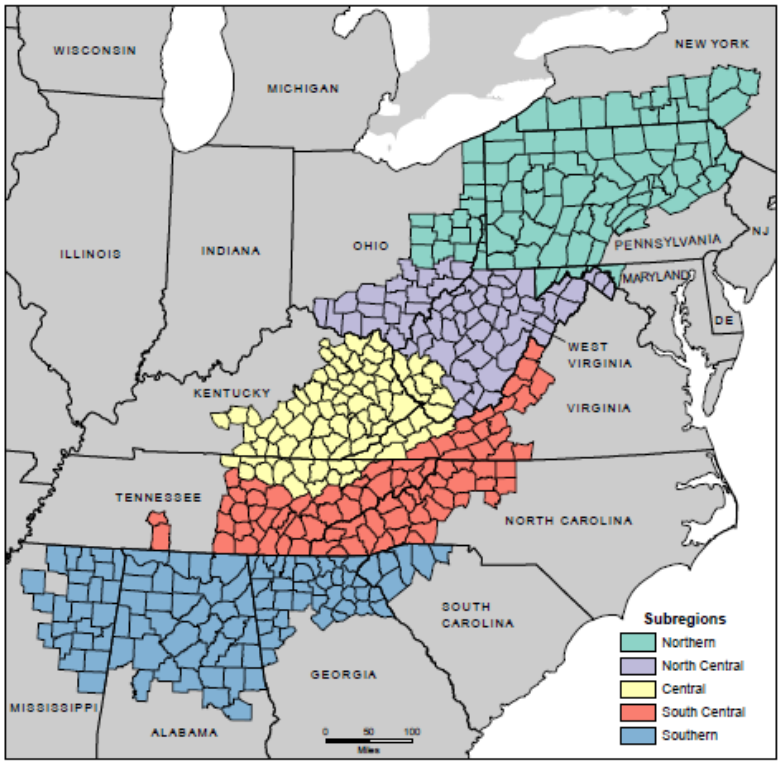




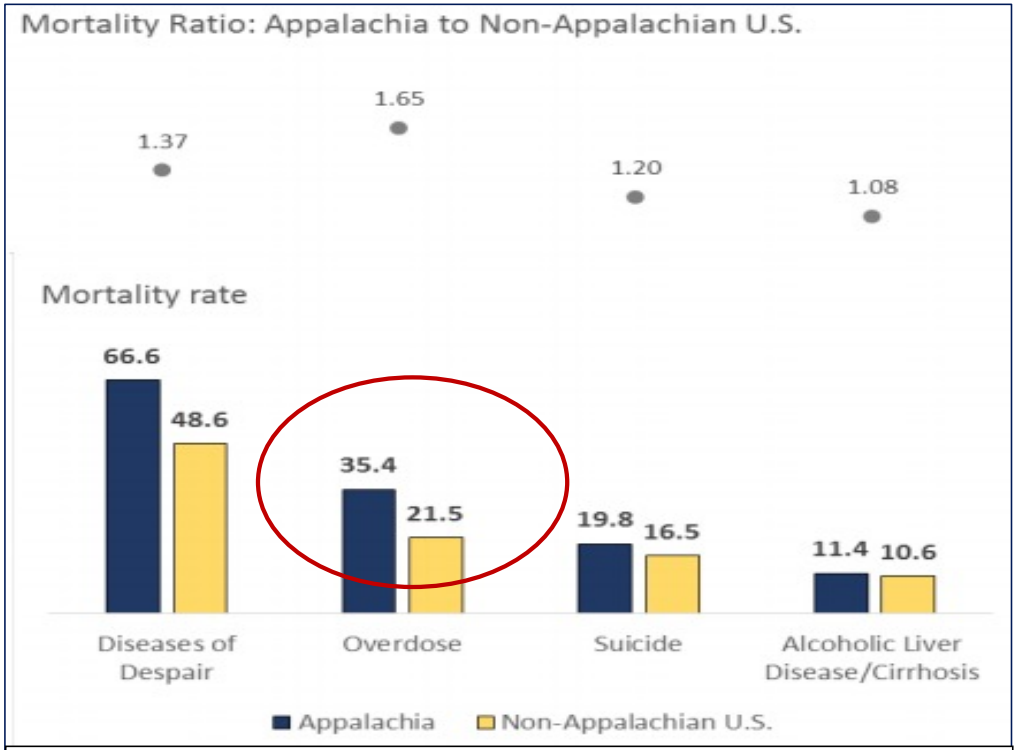
HEALTH

White House Panel Recommends Declaring National Emergency on Opioids

By ABBY GOODNOUGH JULY 31, 2017



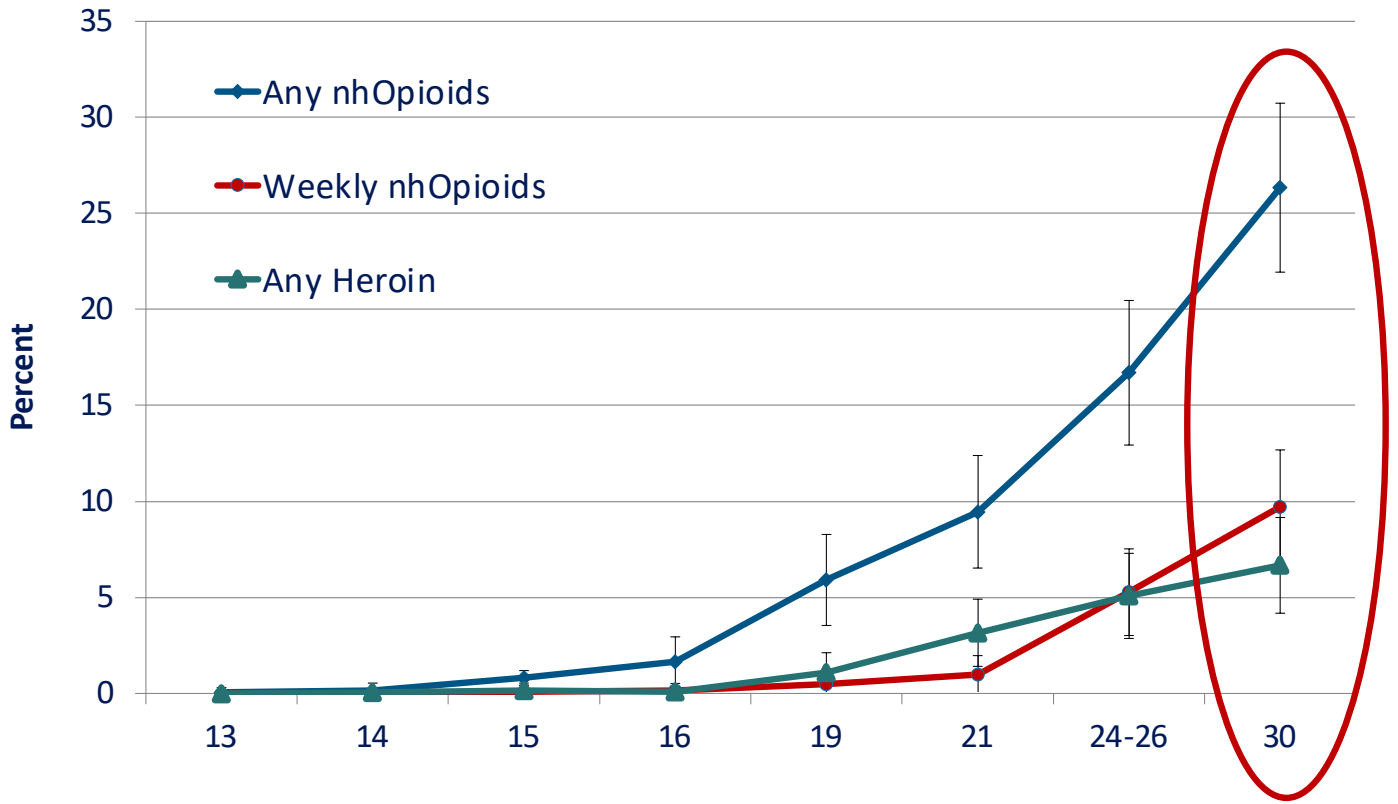
Data source: Appalachian Regional Commission, Created November 2009

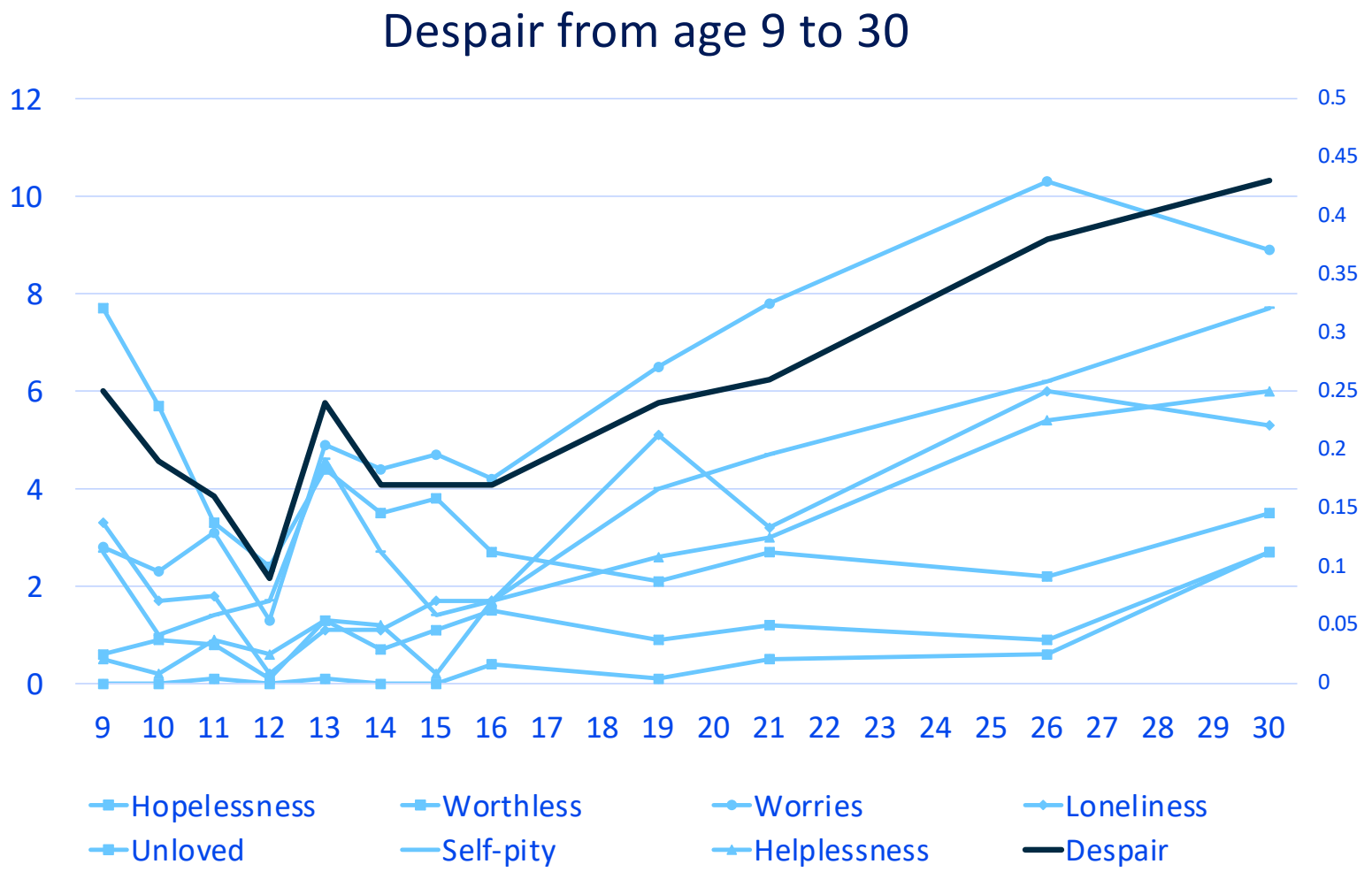


Appalachian deaths of despair from Meit et al. 2017.

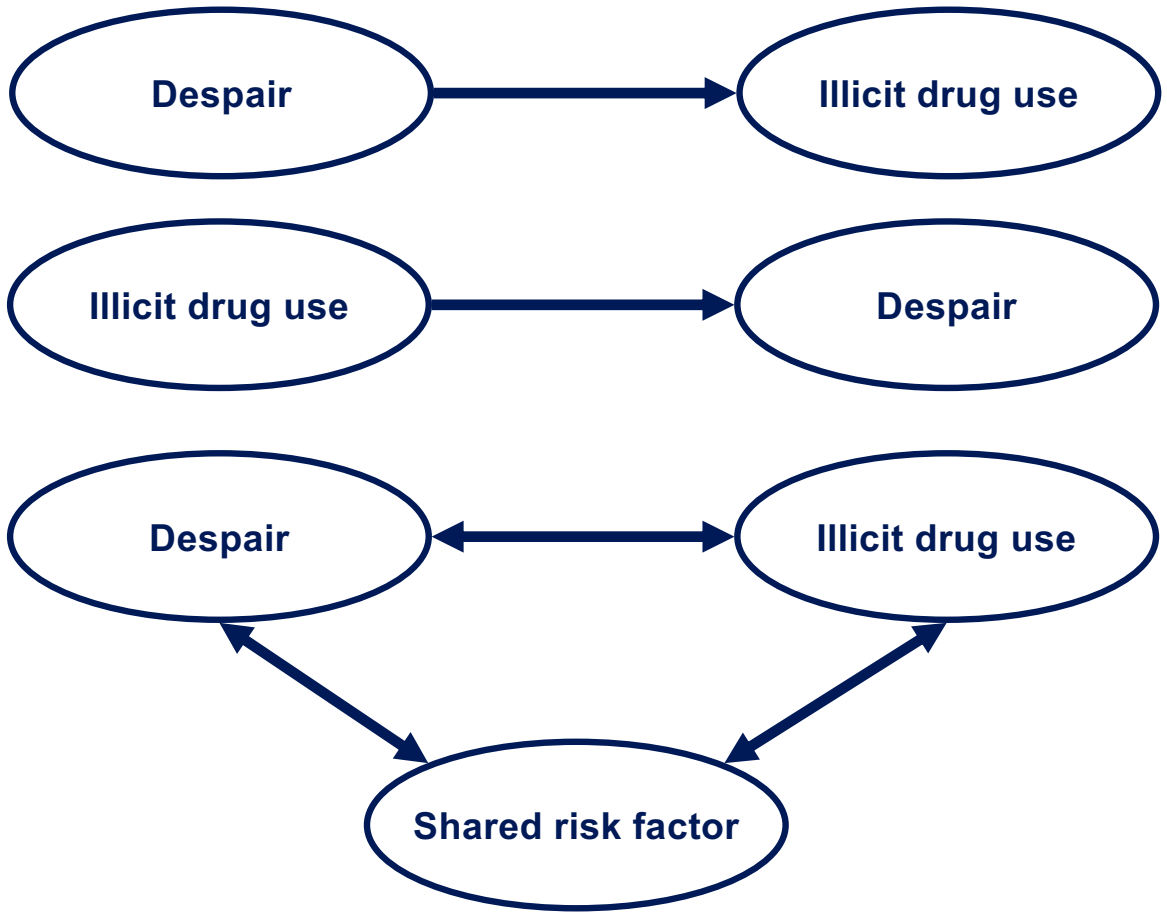
Meit, M., Hefferman, M., Tanenbaum, E., & Hoffmann, T. (2017). *Final report: Appalachian diseases of despair*.

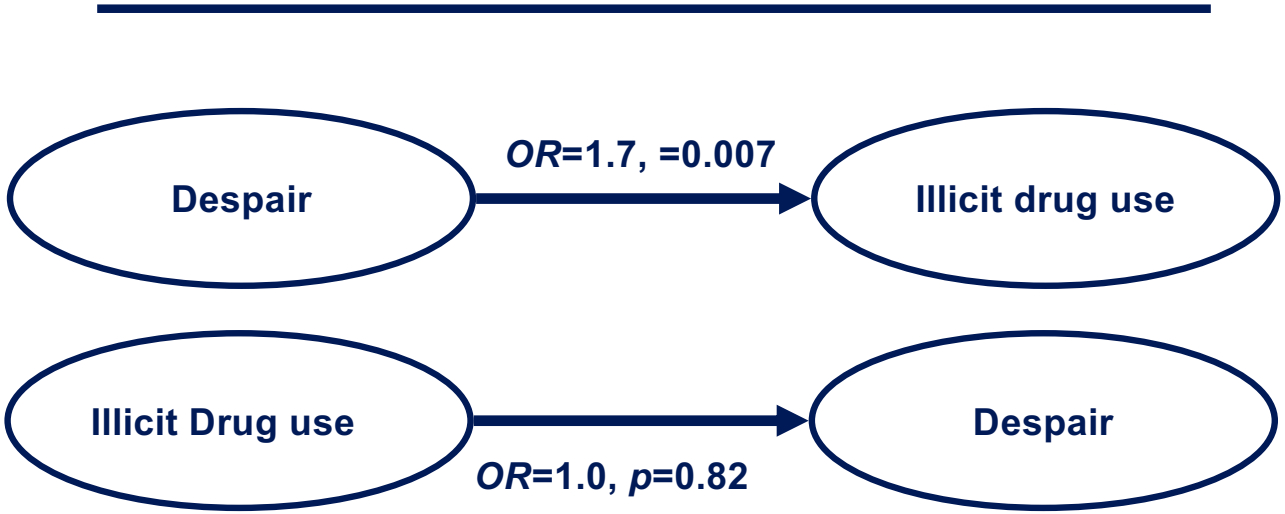
Opioid Use from age 9 to 30




Despair from age 9 to 30
12
10
8
6
4
2
0
0.5
0.45
0.4
0.35
0.3
0.25
0.2
0.15
0.1
0.05
0
9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30
Hopelessness
Worthless
Worries
Loneliness
Unloved
Self-pity
Helplessness
Despair

	Cognitive Despair				
	0	1	2	3+	Unadj.
Total	68.6 (883)	18.4 (212)	6.6 (74)	6.4 (97)	
Sex					
Females	63.9 (383)	20.4 (108)	9.5 (40)	6.2 (50)	--
Males	73.3 (500)	16.4 (104)	3.8 (34)	6.6 (47)	0.07
Race					
White	70.5 (563)	17.3 (164)	6.3 (54)	6.0 (84)	--
AA	36.9 (41)	36.2 (20)	12.6 (12)	14.2 (8)	**<0.001**
AI	87.2 (279)	8.8 (28)	2.5 (8)	1.6 (5)	**<0.001**
Education					
No HS degree	55.4 (94)	22.4 (22)	12.8 (10)	9.5 (16)	**0.003**
HS only	60.2 (172)	22.8 (46)	5.3 (9)	11.8 (25)	**0.009**
Some college	69.1 (290)	13.9 (68)	8.8 (37)	8.2 (42)	**0.05**
4 year degree	70.7 (236)	22.0 (61)	5.1 (17)	2.2 (10)	--
Poverty					
Yes	50.7 (234)	25.6 (94)	8.7 (27)	15.0 (64)	**<0.001**
No	76.5 (649)	15.1 (118)	5.7 (47)	2.6 (33)	--


Despair
Illicit drug use
Illicit drug use
Despair
Despair
Illicit drug use
Shared risk factor



Adjusted for sex, race/ethnicity, educational status, partner, parent, Poverty, and **time 1 status on outcome variable**

Diseases Predicting Later Despair

Association of cognitive despair with psychiatric and substance "diseases" (ages 25 and 30)					
Lagged predictor	Outcome	OR	95% CI	p	Covars
Suicide	Cognitive despair	0.9	0.5-1.4	0.52	2, 6
Alcohol disorder	Cognitive despair	0.8	0.5-1.2	0.28	2, 6
Illicit drug use	Cognitive despair	1.0	0.7-1.5	0.82	2, 6

Covariates included: 1 = sex, 2 = race/ethnicity, 3 = educational status, 4 = partner, 5 = parent, 6 = poverty,

Despair Predicting Later Diseases

Association of cognitive despair with psychiatric and substance "diseases" (ages 25 and 30)					
Lagged predictor	Outcome	OR	95% CI	p	Covars
Cognitive despair	Suicide	**1.5**	**1.1-2.0**	**0.02**	1, 3, 6
Cognitive despair	Alcohol disorder	0.8	0.6-1.2	0.31	1, 2
Cognitive despair	Illicit drug use	**1.7**	**1.2-2.5**	**0.007**	4, 6

Covariates included: 1 = sex, 2 = race/ethnicity, 3 = educational status, 4 = partner, 5 = parent, 6 = poverty,

JAMA Network | Open

Original Investigation | Public Health

Associations of Despair With Suicidality and Substance Misuse Among Young Adults

William E. Copeland, PhD; Lauren Gaydosh, PhD; Sherika N. Hill, PhD; Jennifer Godwin, PhD; Kathleen Mullan Harris, PhD; E. Jane Costello, PhD; Lilly Shanahan, PhD

Abstract

IMPORTANCE *Deaths of despair* is a term that has recently been used to describe the increases in premature mortality from suicides, drug overdoses (particularly from opiates), and alcohol-related liver disease among US adults. Despite the use of the term *despair*, its role in these causes of premature death has not been empirically tested.

OBJECTIVE To test whether despair among young adults is associated with suicidal thoughts and behavior, alcohol misuse, and drug misuse.

DESIGN, SETTING, AND PARTICIPANTS The Great Smoky Mountains Study is a Southeastern, mixed urban-rural population-based cohort study conducted from November 10, 1992, to September 22, 2015. A total of 1420 participants originally 9, 11, and 13 years of age were followed up 11 times to 30 years of age (11 230 person-observations). A total of 1154 of 1400 living participants (82.4%) were assessed at 30 years of age. Statistical analysis was performed from May 7, 2019, to April 10, 2020.

EXPOSURES Participants were assessed with structured interviews for indicators of despair (eg, hopelessness, helplessness, low self-worth, and feeling unloved). Despair was assessed with items from structured interviews: the Child and Adolescent Psychiatric Assessment and the Young Adult Psychiatric Assessment.

MAIN OUTCOMES AND MEASURES Structured interviews were used to assess suicidal thoughts and behavior, substance use, and *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) alcohol use disorder and drug use disorder (including opioids) in young adulthood (2424 observations of 1266 individuals between 25 and 30 years of age).

Key Points

Question Is despair associated with drug or alcohol misuse or suicidal thoughts and behaviors among young adults?

Findings In this population-based cohort study in rural Appalachia, despair was longitudinally associated with higher rates of suicidal thoughts and behavior, illicit drug use, and opioid use, even after adjusting for sociodemographic factors, prior outcome status, and prior depressive disorder status; despair was not associated with alcohol use disorder. There was no consistent pattern of moderation by race/ethnicity, poverty status, sex, or educational level.

Meaning Despair early in life is longitudinally associated with several (but not all) putative despair-related diseases.

Population Research and Policy Review (2025) 44:33
https://doi.org/10.1007/s11113-025-09952-4

ORIGINAL RESEARCH

The Role of Despair in Predicting Self-Destructive Behaviors

Lauren Gaydosh[1] · Audrey Kelly[2] · Iliya Gutin[3] · Lilly Shanahan[4] · Jennifer Godwin[5] · Kathleen Mullan Harris[1] · William Copeland[6]

Received: 15 May 2024 / Accepted: 17 March 2025 / Published online: 13 May 2025

Abstract

Working age (25–64) mortality in the US has been increasing for decades, driven in part by rising deaths due to drug overdose, as well as increases in suicide and alcohol-related mortality. These deaths have been hypothesized by some to be due to despair, but this has rarely been empirically tested. For despair to explain mortality due to alcohol-related liver disease, suicide, and drug overdose, it must first predict the behaviors that lead to such causes of death. To that end, we aim to answer two research questions. First, does despair predict the behaviors that are antecedent to the "deaths of despair"? Second, what measures and domains of despair are most important? We use data from over 6000 individuals at five waves of the National Longitudinal Study of Adolescent to Adult Health and apply supervised machine learning to assess the role of despair in predicting self-destructive behaviors associated with these causes of death. Comparing predictive performance within each outcome using measures of despair to benchmark models of clinical and prior behavioral predictors, we evaluate the added predictive value of despair above and beyond established risk factors. We find that despair underperforms compared to clinical risk factors for suicidal ideation and heavy drinking, but over performs compared to clinical risk factors and prior behaviors for illegal drug use and prescription drug misuse. We also compare model performance and feature importance across outcomes; our ability to predict thoughts of suicide, drug abuse and misuse, and heavy drinking differs depending on the behavior, and the relative importance of different indicators of despair varies across outcomes as well. Our findings suggest that the self-destructive behaviors are distinct and the pathways from despair to self-destructive behavior varied. The results draw into question the relevance of despair as a unifying framework for understanding the current crisis in midlife health and mortality.

Keywords Despair · Substance use · Alcohol use · Suicide · Machine learning

Mortality Data in GSMS (as of 2023)	GSMS (N=1420)	
	n	Wgted %
Alive	1330	96.28
Dead		
All cause	90	3.72
DoD	39	1.60
Car accidents and Homicide	14	0.57
DoD plus Car accidents and Homicide	53	2.17
Specific causes		
overdose	28	1.34
suicide	7	0.20
alcohol-related	4	0.06
car accident	11	0.47
homicide	3	0.10
accidental injury	5	0.11
illness	32	1.44

Child Mental health and All Cause Mortality

	HR	p	se	z	95% CI	
Male	0.97	0.95	0.42	-0.06	0.41	2.29
Parent Ed	0.89	0.06	0.05	-1.89	0.80	1.00
Black	1.54	0.53	1.05	0.63	0.40	5.85
Am. Indian	2.77	0.00	0.93	3.04	1.44	5.34
CD Symptoms	**1.58**	**0.00**	**0.22**	**3.25**	**1.20**	**2.08**
MDD Symptoms	1.32	0.24	0.32	1.17	0.83	2.12

CD = symptoms of conduct disorder (aggressive behavior and delinquency)
MDD = symptom of depressive disorders (depressed mood, worthlessness, physical symptoms)

Child Mental health and Deaths of Despair

	HR	p	se	z	95% CI	
Male	0.90	0.87	0.60	-0.16	0.24	3.30
Parent Ed	0.85	0.04	0.07	-2.10	0.72	0.99
Black	0.00	0.00	0.00	-36.03	0.00	0.00
Native Amer	2.47	0.07	1.24	1.80	0.92	6.58
CD Symptoms	**1.70**	**0.00**	**0.25**	**3.63**	**1.28**	**2.26**
MD Symptoms	**1.78**	**0.02**	**0.45**	**2.29**	**1.09**	**2.92**

CD = symptoms of conduct disorder (aggressive behavior and delinquency)
MDD = symptom of depressive disorders (depressed mood, worthlessness, physical symptoms)

Tentative conclusions

- Term “deaths of despair” should be retired
- On an individual level, however, despair is associated with suicidality and illicit drug use
- Premature mortality in southeastern Appalachia is high
- Multiple types of early mental health problems – both emotional and behavioral - are associated with premature mortality

Acknowledgements

GSMS collaborators: Jane Costello, Adrian Angold, Wanda Burns, and Rebecca Woodward

GSMS select funding for this work: R01MH117559, R01DA03652, R03MH094605, R01DA011301, R01DA016977, R01MH063970, RO1HD29409, R01HD32336

GSMS participants, their parents, GSMS field staff!!

Further Questions or Suggestions related to GSMS-RA & Mid-Life Health Inequalities study, please contact:

- Bill Copeland (William.Copeland@med.uvm.edu)
- Kate Cagney (kcagney@umich.edu)
- Naomi Duke (naomi.duke@duke.edu)
- Joe Hotz (hotz@uchicago.edu)

Already collected

- 12,000+ assessments of 1420 individuals from age 9 to the late 30s
- Community-representative
- Administrative records and geospatial data linkage
- Low attrition (>80% participation rate across 12 assessment waves)
- 7000+ banked dried bloodspots
- Longitudinal assays of hormones, and stress biomarkers complete
- 800k DNA genotyping complete; whole genome methylation sequencing

Data collection in early 40s

- Survey of health, health risk, social, and economic functioning
- Cognitive assessment
- Physical performance assessment
- Bloodspots and biomeasure
- Everyday life and rural context:
  - 6-month EMA protocol
- Harmonized measures, codebooks and datasets

Duke