



“Lives of despair” at risk for “deaths of despair”: tracking an under-recognized, vulnerable population

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Abstract

Purpose The substantial and unexpected increase in “deaths of despair” in the US (e.g., deaths from drug overdose, suicide, and alcohol-related liver diseases) reported by economists Case and Deaton in 2015 raises questions about the number and characteristics of US adults potentially living “lives of despair” with these problems.

Methods We used data from the National Epidemiologic Survey on Alcohol and Related Conditions Wave III (NESARC-III) to examine population estimates and characteristics of adults with lifetime history of substance use disorder (SUD) and suicide attempt, or either condition alone, as compared to those with neither.

Results An estimated 7.2 million adults had both lifetime SUD and suicide attempt and 78.8 million had either. Those with both faced far more psychosocial adversities, familial adverse experiences and psychiatric disorders compared to those with the other two groups, and reported greater mental health service utilization. Multivariable analysis showed that psychiatric multimorbidity and violence were the strongest correlates of having both conditions as compared to neither while those with either condition fell in between.

Conclusion A substantial number of US adults live with a lifetime SUD and suicide attempt with a multiplicity of additional socioeconomic, psychiatric and familial problems. While their utilization of mental health care service exceeds those with either or neither conditions, quality of life remained much poorer, suggesting that mental health treatment alone may not be enough to mitigate their sufferings, and a combination of both social policy support and quality mental health care may be needed.

Keywords Suicide · Substance use disorder · Alcohol use disorder · Multimorbidity

Introduction

The concept of “deaths of despair,” was introduced by economists Anne Case and Angus Deaton in 2015 to characterize the unexpected increase in US mortality rates during the 2000s, reversing a century of unbroken decline [1]. This increase especially affected middle-aged non-Hispanic

Whites without a college degree, and was prominently associated with alcohol and drug overdose, suicide, and alcohol-related liver disease [1–3]. In this particular demographic, from 1999 to 2013, deaths by overdose and suicide increased by 44 and 17 per 100,000, respectively, and continue to climb [1, 2]. Further, this trend is now extending across other middle-aged racial and ethnic groups in the US [4–6], with suicide and overdose combining to become the seventh leading cause of death in 2019, marking a 174% increase from 41,364 in 2000 to 113,259 in 2019 [7, 8]. Many opioid overdose deaths also may, in fact, reflect an underlying suicidal intent [9, 10], and the overall toll may be further exacerbated by the psychological shockwave of the COVID-19 pandemic [11–13].

While Case and Deaton focused on increasing death rates as indicators of growing socioeconomic suffering among a broad segment of the US population, the numbers they reported were inherently of small magnitude, reported in

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deaths per 100,000 persons [14]. However, the increasing rates of “deaths of despair” raises the alarming suggestion that a growing number of people are suffering from “lives of despair” with substance use disorders (SUD) [8], suicidal impulses and, presumably, associated mental illnesses [15]. Further, this trend likely reflects the changing states of well-being in some parts of the US, such that the “deaths of despair” are the visible part of the iceberg, which is a function of the total population living “lives of despair.” The “deaths of despair” concept, emerging from economics and epidemiology, was not borne from a clinical perspective, and did not focus on what the increasing death rate meant for those who did not *die* from these conditions, but rather are living or have lived with them. It is thus unknown how many people are suffering from such day-to-day “lives of despair” in the general population, the full range of problems they face, and whether they have used mental health services.

While Case and Deaton described changes in the incidence of individual causes of death, they did not examine broad correlates of suffering associated when these conditions occur together. Recent studies have demonstrated substantial adverse effects of behavioral “multimorbidity;” in other words, multiple psychiatric disorders are associated with multiple adverse social conditions (e.g., homelessness or incarceration), and such multimorbidity is more frequently encountered by clinicians than single conditions by themselves [16, 17]. The broadening of perspective to the general populations allows exploration of the additional suggestion by Case and Deaton that the high cost of private health insurance and resultant inadequate access to health care, along with deteriorating socioeconomic conditions may be major reasons that deaths of despair have emerged out of lives of despair. A more extensive examination of this population, the multiplicity of their problems, and their use of services thus seems timely.

Previously, studies using nationally representative surveys such as the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) have helped to assess and characterize the prevalence and correlates of suicide attempts as well as SUD in the US population [18–21]. Further, inspired by Case and Deaton, recent studies have examined the change in morbidity and distress using nationally representative US data [22–24]. However, to our knowledge, no study has investigated the subpopulation who live with both conditions (i.e., lifetime suicide attempt and SUD) using the NESARC-III, and few studies to date have approached “deaths of despair” from a psychiatric and mental health research perspective [25]. To address this gap in knowledge, we used nationally representative survey data from the NESARC-III [26, 27] conducted in 2012–2013, during the main period studied by Case and Deaton [1] to extend their alarming findings on “deaths of despair” to a study of “lives of despair” by estimating the numbers and concurring adversities of people who have lived with drug and/

or alcohol use disorders and suicidality. We compared the estimated numbers along with the sociodemographic, behavioral, and diagnostic characteristics, of adults who have experienced: (1) both lifetime SUD and suicide attempt; (2) either lifetime SUD or suicide attempt; and (3) neither SUD nor suicide attempt. We have selected lifetime as opposed to past-year SUD and suicide attempt, because this study is focusing on the burden of those living “lives of despair” rather than contemporary suicidality and/or SUD.

Following Case and Deaton, we hypothesized that the number of US adults living “lives of despair” would be substantial and would more likely be non-Hispanic White, with a multiplicity of sociodemographic problems and mental health disorders. We further hypothesized that those who had experienced both SUD and suicide attempt would suffer numerous additional adversities and that they would be less likely to have received mental health treatment than others, especially after adjusting for their greater level of need. Based on the theoretical framework posited by Case and Deaton and previous literature on suicidal behavior and SUD [18–21], we had the opportunity to examine a comprehensive range of sociodemographic, social, and clinical characteristics in our analyses. Further, we have examined a comprehensive adjusted rates of mental health service use to test our hypothesis on under-utilization of mental health treatment.

Methods

Data source and study sample

Data were from the NESARC-III, a nationally representative survey of non-institutionalized civilian population of the US aged 18 years and older, conducted between April 2012 and June 2013, sponsored by the National Institute of Alcohol Abuse and Alcoholism. Information on alcohol and drug use disorders, and medical and psychiatric comorbidities were collected using the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5) [26]. Details of the survey are available on the NESARC-III website [27].

The current study was approved by the institutional review boards at the US National Institutes of Health, Yale School of Medicine and the VA Connecticut Healthcare System. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline [28].

Measures

Lifetime suicide attempt

Suicide attempt was assessed using a single questionnaire, “Have you ever attempted suicide?”

Lifetime SUD

Lifetime SUD was assessed by the AUDADIS-5, a structured, computer-assisted diagnostic interview based on the diagnostic criteria for SUD in the *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (DSM-5) [29]. Lifetime SUD include: alcohol, opioid, cannabis, cocaine/crack, sedative/tranquillizer, club drug, inhalant/solvent, stimulant, heroin, and other use disorders.

Sociodemographic characteristics

Study participants reported their age, gender, race/ethnicity, marital status, employment, annual household income, nativity (born in the US or outside the US), education, health insurance coverage, urban residence, and veteran status.

Behavioral characteristics. Information on incarceration, trouble with police, homelessness, parental history, childhood adverse experiences (ACEs), experience of discrimination, and attendance at religious services were examined.

Violent behavior score was based on a reported history of seven types of violence toward others since the age of 15 and following Harford et al. [30] represented the sum of seven dichotomous items: (1) ever steal something from someone, like mugging them, threatening them with a weapon, or taking their purse/wallet; (2) ever force anyone to engage in any sexual activity with you against their will; (3) ever get into a lot of fights that you started; (4) ever physically hurt another person in any way on purpose; (5) ever get into a fight that came to swapping blows with someone intimate; (6) ever use a weapon in a fight; and (7) ever hit someone so hard that you injured them [30].

Childhood neglect (range 0–45) was measured based on the sum of a subset of items from the conflict tactics scales [31] that were rated by a 5-point ordinal scale, with higher scores indicating more frequent experiences.

Sexual abuse (range 0–20) was assessed using the sum of items from the childhood trauma questionnaire [32] that were rated by a 5-point ordinal scale, with higher scores indicating more frequent experiences.

Health-related quality of life (HRQOL) was assessed with the Short Form 12 (SF-12), a 12-item standardized questionnaire with algorithm-based scores ranging from 0 to 100 for both a mental health component score (MCS) and a physical health component score (PCS) with higher scores indicating better HRQOL [33]. Both are standardized to the US population with a mean of 50 and standard deviation of 10.

Social support was measured using the Interpersonal Support Evaluation List (ISEL-12) [34], which averages 12-items rated on a 4-point severity scale with higher scores indicating greater social support.

Social contact was measured by the sum of three self-reported questions that asked respondents the number of

family, friends and other acquaintances with whom they had meaningful contact in the past two weeks.

Quality-adjusted life years (QALYs) were assessed following the published algorithm for combining items from the SF-12 ranging from 0.0 (death) to 1.0 (perfect health) [35, 36].

Past-year psychiatric and SUD diagnoses

Past-year SUD was assessed by the AUDADIS-5 for SUDs including alcohol, opioid, cannabis, cocaine, and sedative use disorders. Past-year psychiatric disorders were also assessed using the AUDADIS-5, based on DSM-5 criteria, for major depressive disorder (MDD) and dysthymia (persistent depressive disorder), of particular relevance to issues of subjective despair and other DSM-5 non-substance use diagnoses. Multimorbidity of psychiatric disorder and SUD were each represented by one dichotomous variable representing the presence of only one past-year diagnosis and the others indicating two or more diagnoses.

Service use. Self-reported lifetime receipt of any psychiatric treatment and/or SUD treatment was documented. Involvement in self-help groups [e.g., Alcoholics Anonymous (AA) and Narcotics Anonymous (NA)] and consultation with clergy for SUD were also documented. A measure reporting that the respondent did not receive SUD treatment although they felt that they needed it was also documented.

Physical conditions

Medical comorbidities were measured by the sum of 18 individual dichotomously reported medical conditions (e.g., arthritis, diabetes, and cancer) ranging from 1 to 18. Moderate/severe pain in the past 4 weeks was based on the highest two of five rating levels in pain item from the SF-12.

Statistical analysis

Differences across those with (1) both lifetime suicide attempt and SUD, (2) either lifetime suicide attempt or SUD, and (3) neither lifetime suicide attempt and SUD were evaluated using effect sizes (Cohen's d or relative risk [RR]) rather than p values because large sample sizes involved in this study can result in statistical significance even for very small, trivial differences. Instead, effect sizes were used where RR of > 1.5 or < 0.67 deemed to represent substantial effects for dichotomous variables [37] and Cohen's d of > 0.2 or < -0.2 considered to represent at least small effect sizes for continuous variables [38].

Multivariable-adjusted logistic regression analyses with backward selection were then used to identify factors that independently differentiated pairs of the three groups. These analyses included all variables that were identified

as showing substantial differences on bivariate analysis. We have adopted the principal of superordinate variables such that when subordinate variables (e.g., opiate use disorder) are components of superordinate categories we use the superordinate category rather than both to avoid multicollinearity issues. Since both categorical and continuous variables were included, standardized regression coefficients (SRCs) were used to compare magnitudes of effect between variables.

Differences in service use were also examined with stepwise logistic regressions comparing pairs of groups net of factors previously identified as differentiating the groups. Post-stratification NESARC-calculated weights were applied for all analyses. Data analyses were conducted using SAS statistical program version 9.4 [39].

Results

Among the total sample ($n = 36,171$ respondents representing 248 million adults), 3.13% ($n = 1133$, representing 7.2 million US adults) reported both a history of lifetime SUD and suicide attempt (*lifetime SUD and suicide attempt group*). An additional 29.3% ($n = 10,594$ representing 78.8 million adults) reported either lifetime SUD or suicide attempt (*lifetime SUD or suicide attempt group*). 67.6% ($n = 24,444$, representing 167.6 million US adults) did not report any history of SUD or suicide attempt (*neither group*). Respondents who reported a history of hallucinogen use disorder were excluded ($n = 138$).

Sociodemographic characteristics by lifetime suicide attempt and SUD

Those in the *despair group* were relatively younger, more likely to be White compared to those with the *neither group* and also less likely to be married or to have private insurance, but more likely to be separated/divorced, unemployed, to have lower income or be covered by Medicaid and half as likely to have a college degree compared to those in the *lifetime SUD or suicide attempt group* and the *neither group* (Table 1).

Behavioral characteristics

Those in the *lifetime SUD and suicide attempt group* were most likely to have a history of incarceration, trouble with police over the past year, more violent behaviors, past year homelessness, parental adverse histories, ACEs, and to report having experienced discrimination followed by those in the *lifetime SUD or suicide attempt group* and then the *neither group*. These monotonic trends were consistent across all measures.

Regarding protective social measures, a reverse trend was observed with those in the *lifetime SUD and suicide attempt group* being the least likely to have social contacts/support or to participate in religious services, and having lowest scores on measures of HRQOL. However, the differences between those in the *lifetime SUD or suicide attempt group* and the *neither group* were less pronounced on these measures (Table 2).

Diagnostic characteristics and service use

The gradients observed above continued to be pronounced in terms of psychiatric diagnoses (including depressive disorders), SUD diagnoses, mental health treatment history, medical comorbidities, and pain. Those in the *lifetime SUD and suicide attempt group* were the most likely to have multiple morbidities (i.e., psychiatric diagnoses, physical conditions), followed by those in the *lifetime SUD or suicide attempt group* and the *neither group*. This trend extended to frequency of lifetime service mental health use as well (Table 3).

Multivariable logistic regression models

Multivariable stepwise logistic regression with backward selection (Table 4) showed that those in the *lifetime SUD and suicide attempt group*, differed significantly and independently from those in both the *lifetime SUD or suicide attempt group* and the *neither group*, in having experienced past year homelessness, parental drug or suicide attempts, childhood neglect or sexual abuse, more violent behavior, multiple past year psychiatric diagnoses and medical comorbidities. Those in the *lifetime SUD and suicide attempt group* when compared to the *lifetime SUD or suicide attempt group* were more likely to have a history of parental alcohol use problem, any trauma or discrimination, and past year psychiatric diagnoses. Those in the *lifetime SUD and suicide attempt group* were less likely to be Black, married, and to participate in religious services compared to those in the *neither group*.

Those in the *lifetime SUD or suicide attempt group* were more likely to report violent behaviors compared to those in the *neither group* while those in the *lifetime SUD and suicide attempt group* and the *lifetime SUD or suicide attempt group* were younger, and more likely to have been incarcerated when compared to those in the *neither group*.

There were fewer differences between those in the *lifetime SUD and suicide attempt group* and the *lifetime SUD or suicide attempt group* than between the *lifetime SUD and suicide attempt group* and the *neither group*. Those in the *lifetime SUD and suicide attempt group* were more likely to be separated/divorced, covered by Medicaid, and less likely to hold a college degree, to be retired, and had

Table 1 Sociodemographic characteristics in US adults by lifetime suicide attempt and SUD

Variable	(1) Suicide attempt and SUD (<i>n</i> = 1133; 3.1%)	(2) Suicide attempt or SUD (<i>n</i> = 10,594; 29.3%)	(3) No Suicide attempt/ SUD (<i>n</i> = 24,444; 67.6%)	(1) vs. (2)	(1) vs. (3)	(2) vs. (3)
				RR or <i>d</i>	RR or <i>d</i>	RR or <i>d</i>
Age, mean (SD)	40.0 (13.5)	42.0 (15.5)	48.9 (18.4)	− 0.11	− 0.51 ^b	− 0.39 ^b
Male Gender (%)	39.6	58.6	43.6	0.68	0.91	1.34
Race (%)						
Non-Hispanic white	74.6	72.9	62.7	1.02	1.19	1.16
Non-Hispanic black	8.50	9.78	12.84	0.87	0.66 ^a	0.76
Hispanic	10.8	12.2	16.1	0.88	0.67	0.76
Other	6.04	5.11	8.33	1.18	0.73	0.61 ^a
Marital status (%)						
Married	33.3	44.7	55.0	0.74	0.60 ^a	0.81
Never married	28.4	27.3	20.1	1.04	1.41	1.36
Separated/divorced	24.1	15.8	12.4	1.53 ^a	1.94 ^a	1.27
Widowed	2.35	2.41	7.50	0.97	0.31 ^a	0.32 ^a
Employment status (%)						
Employed	67.7	78.1	66.5	0.87	1.02	1.18
Unemployed (disability)	17.1	5.98	4.32	2.86 ^a	3.96 ^a	1.38
Unemployed (no disability)	14.0	9.54	6.14	1.46	2.28 ^a	1.55 ^a
Retired	4.97	10.1	21.5	0.49 ^a	0.23 ^a	0.47 ^a
Income (%)						
< \$20,000	37.6	22.7	22.1	1.65 ^a	1.70 ^a	1.03
\$20,000–39,999	26.4	23.3	24.4	1.13	1.08	0.96
\$40,000–59,999	17.9	22.3	22.1	0.80	0.81	1.01
≥ \$60,000	18.1	31.6	31.4	0.57 ^a	0.58 ^a	1.01
Born in U.S. (%)	94.8	92.3	79.8	1.03	1.19	1.16
Education (%)						
Less than high school	16.4	10.3	14.1	1.60 ^a	1.17	0.73
High school or equivalent	27.8	25.9	25.6	1.08	1.09	1.01
Some college	39.9	35.4	31.7	1.13	1.26	1.12
College or higher	15.8	28.3	28.6	0.56 ^a	0.55 ^a	0.99
Health insurance (%)						
Private	45.4	59.9	57.5	0.76	0.79	1.04
Medicare	17.7	14.1	24.9	1.26	0.71	0.57 ^a
Medicaid	22.9	10.7	9.53	2.14 ^a	2.41 ^a	1.12
Any insurance	76.7	79.3	81.0	0.97	0.95	0.98
Other factors (%)						
Urban residence	77.7	79.2	78.6	0.98	0.99	1.01
Veteran status	8.97	11.3	9.03	0.80	0.99	1.25

*d*Cohen's *d*, *RR*risk ratio, *SD*standard deviation, *SUD*substance use disorder

^aRefers to *RR* > 1.5 or < 0.67

^bRefers to Cohen's *d* > 0.2 or < − 0.2

fewer social contacts. Those in *the lifetime SUD or suicide attempt group* in comparison to those in *the neither group* were more likely to be unemployed due to disability and to have had trouble with the police, whereas those in *the neither group* was more likely to be covered by Medicare.

Mental health service use

On bivariate analysis, respondents in *the lifetime SUD and suicide attempt group* were almost twice as likely to receive any mental health treatment compared to those in

Table 2 Behavioral characteristics in US adults by lifetime suicide attempt and SUD

Variable	(1) Suicide attempt and SUD (<i>n</i> = 1133; 3.1%)	(2) Suicide attempt or SUD (<i>n</i> = 10,594; 29.3%)	(3) No suicide attempt/ SUD (<i>n</i> = 24,444; 67.6%)	(1) vs. (2)	(1) vs. (3)	(2) vs. (3)
				RR or <i>d</i>	RR or <i>d</i>	RR or <i>d</i>
History of incarceration (%)						
Before 15	16.4	7.19	1.93	2.28 ^a	8.47 ^a	3.72 ^a
After 15	32.9	20.8	4.95	1.59 ^a	6.65 ^a	4.19 ^a
PY trouble with police (%)	6.54	3.22	0.65	2.03 ^a	10.13 ^a	5.00 ^a
Violent behavior 1–7, mean (SD)	1.66 (1.62)	0.98 (1.31)	0.27 (0.72)	0.70 ^b	1.43 ^b	0.73 ^b
PY homelessness (%)	10.5	2.61	0.63	4.02 ^a	16.53 ^a	4.11 ^a
Parental history (%)						
Alcohol use	51.8	31.7	18.2	1.64 ^a	2.84 ^a	1.74 ^a
Drug use	25.0	9.01	3.42	2.77 ^a	7.29 ^a	2.63 ^a
Incarceration	24.2	11.2	5.30	2.15 ^a	4.56 ^a	2.12 ^a
Psychiatric hospitalization	19.3	7.19	3.95	2.68 ^a	4.89 ^a	1.82 ^a
Suicide attempt	16.1	4.41	2.06	3.65 ^a	7.81 ^a	2.14 ^a
Death by suicide	3.00	1.17	0.68	2.56 ^a	4.40 ^a	1.72 ^a
Adverse childhood experiences						
Neglect, mean (SD)	18.7 (9.03)	13.6 (5.83)	11.7 (4.62)	0.97 ^b	1.34 ^b	0.37 ^b
Sexual abuse, mean (SD)	6.61 (4.20)	4.57 (1.95)	4.32 (1.45)	1.16 ^b	1.31 ^b	0.14
Repeated trauma (%)	23.6	16.5	11.9	1.43	1.99 ^a	1.39
Witnessed trauma (%)	73.9	61.6	44.7	1.20	1.65 ^a	1.38
Any trauma (%)	83.7	61.0	42.9	1.37	1.95 ^a	1.42
Any discrimination (%)	33.3	23.2	15.6	1.44	2.13 ^a	1.48
Total social contacts past 2 weeks, mean (SD)	12.0 (10.8)	16.1 (14.7)	16.5 (15.4)	−0.28 ^b	−0.30 ^b	−0.02
Social Support (ISEL), mean (SD)	2.76 (0.61)	2.99 (0.49)	3.03 (0.46)	−0.47 ^b	−0.56 ^b	−0.09
Religious service at least once per month (%)	24.4	31.4	46.7	0.78	0.52 ^a	0.67
Health-related Quality of Life						
Mental component summary: SF-12, mean (SD)	40.7 (12.8)	49.0 (10.1)	52.2 (9.2)	−0.87 ^b	−1.20 ^b	−0.33 ^b
Physical component summary, SF-12, mean (SD)	46.3 (12.7)	49.9 (10.5)	49.6 (10.5)	−0.34 ^b	−0.31 ^b	0.03
Quality Adjusted Life Years (EQ-5D), mean (SD)	0.80 (0.15)	0.88 (0.12)	0.90 (0.11)	−0.73 ^b	−0.88 ^b	−0.16

*d*Cohen's *d*, *EQ*EuroQol, *ISEL* interpersonal support evaluation list, *RR*risk ratio, *SA* suicide attempt, *SD* standard deviation, *SF* short form, *SUD* substance use disorder, *PY* past year

^aRefers to $RR > 1.5$ or < 0.67

^bRefers to Cohen's *d* > 0.2 or < -0.2

the lifetime SUD or suicide attempt group, and more than four times more likely than those in the neither group with similar relationships for use of more specified psychiatric and substance use treatment services (Table 1). These differences were even more pronounced in stepwise logistic regression analyses, after adjusting for group differences potentially reflecting a need for such services (Table 5).

Discussion

In an effort to deepen and broaden the discovery by Case and Deaton of the recent, unexpected increase in mortality among a segment of the US population, we found that in 2012, an estimated 7.2 million US adults (3.13% of the

Table 3 Clinical characteristics in US adults by lifetime suicide attempt and SUD

Variable	(1) Suicide attempt and SUD ($n = 1133$; 3.1%)	(2) Suicide attempt or SUD ($n = 10,594$; 29.3%)	(3) No suicide attempt/ SUD ($n = 24,444$; 67.6%)	(1) vs. (2)	(1) vs. (3)	(2) vs. (3)
				RR or d	RR or d	RR or d
Clinical characteristic						
Psychiatric diagnosis, PY (%)						
MDD	47.9	16.4	7.55	2.92 ^a	6.34 ^a	2.17 ^a
Dysthymia	16.3	4.63	1.80	3.51 ^a	9.02 ^a	2.57 ^a
Single diagnosis	25.6	18.5	10.9	1.38	2.36 ^a	1.70 ^a
> 1 diagnosis	46.4	13.1	4.42	3.53 ^a	10.48 ^a	2.97 ^a
SUD diagnosis, PY (%)						
Alcohol	41.5	41.2	0.0	1.01	N/A	N/A
Opioid	7.03	2.21	0.0	3.18 ^a	N/A	N/A
Cannabis	13.4	7.0	0.0	1.92 ^a	N/A	N/A
Cocaine	3.12	0.83	0.0	3.77 ^a	N/A	N/A
Sedative	3.93	0.83	0.0	4.72 ^a	N/A	N/A
Single diagnosis	36.6	40.1	0.0	0.91	N/A	N/A
> 1 diagnosis	14.0	5.93	0.0	2.36 ^a	N/A	N/A
Medical comorbidities, mean (SD)	1.41(1.63)	0.76(1.16)	0.76(1.73)	0.57 ^b	0.56 ^b	0.00
Moderate/severe pain (%)	39.8	22.5	17.9	1.77 ^a	2.22 ^a	1.25
Lifetime service use						
Any mental health treatment (%)	85.3	45.7	18.2	1.87 ^a	4.68 ^a	2.51 ^a
Any psychiatric treatment lifetime (%)	77.0	33.5	16.9	2.30 ^a	4.56 ^a	1.99 ^a
SUD treatment history (%)						
SUD past year	13.5	5.24	0.22	2.58 ^a	N/A	N/A
SUD lifetime	41.6	20.9	2.10	1.99 ^a	N/A	N/A
Ever sought self help	36.9	12.8	4.08	2.88 ^a	N/A	N/A
SUD PY Clergy	23.4	8.22	0.58	2.85 ^a	N/A	N/A
No PY treatment despite needing them	11.3	3.63	0.04	3.13 ^a	N/A	N/A

d Cohen's d , MDD major depressive disorder, PY past year, RR risk ratio, SD standard deviation, SUD substance use disorder

^aRefers to RR > 1.5 or < 0.67

^bRefers to Cohen's d > 0.2 or < - 0.2

US population) had past histories of SUD and a suicide attempt, and an additional 78.8 million adults (29.3% of the US population) had experienced either condition in their lives, totaling to almost one third of the US adult population, paralleling our hypothesis that the number of US adults living “lives of despair” would be substantial. As hypothesized, those who had both conditions (i.e., living “lives of despair”) were suffering from far more socio-behavioral adversities than those with either conditions or without, most notably a higher prevalence of childhood and parental adverse experiences, depressive disorders, psychiatric multimorbidity, social isolation, homelessness, criminal legal system involvement and violent behavior. However, in contrast with our hypothesis, those in *the*

lifetime SUD and suicide attempt group were also more likely to have used mental health services compared to those living with neither condition, while those with either fell in between the extremes.

It is noteworthy that our finding of 3.13% of the US population having histories of both SUD and suicide attempt(s) exceeds the previously estimated prevalence of lifetime suicide attempts of 2.4% among respondents with or without SUD in previous NESARC-based studies [18]. As economists, Case and Deaton were mainly focused on current socioeconomic and social policy environment that they infer have led to the increase of “deaths of despair,” especially among less educated Whites. They identified the roots of such deaths in diminishing availability of well-paying secure

Table 4 Multivariate regression analysis comparing those who had both lifetime suicide attempt and SUD, to either, or to neither groups

Variable	Group 1 vs 3		Group 1 vs 2		Group 2 vs 3		Paired comparisons
	OR (95% CI)	SRC	OR (95% CI)	SRC	OR (95% CI)	SRC	
Sociodemographic							
Age	0.98 (0.97–0.98)***	–0.232	NS		0.98 (0.98–0.98)***	–0.175	1, 2 < 3
Black race	0.40 (0.32–0.51)***	–0.209	NS		NS		1 < 3
Other race	NS		NS		0.72 (0.65–0.81)***	–0.044	2 < 3
Married	0.69 (0.58–0.83)***	–0.100	NS		NS		1 < 3
Widowed	0.45 (0.28–0.72)***	–0.123	NS		0.68 (0.60–0.78)***	–0.055	1, 2 < 3
Separated/divorced	NS		1.23(1.05–1.44)*	0.046	NS		1 > 2
Unemployed disability	NS				1.31 (1.18–1.46)***	0.035	2 > 3
Retired	NS		0.72 (1.05–1.44)*	–0.052	NS		1 > 2
Education (college or higher)	NS		0.79 (0.65–0.96)*	–0.56	NS		1 > 2
Medicare	NS				0.88 (0.81–0.96)**	–0.028	2 < 3
Medicaid	NS		1.25 (1.06–1.48)*	0.044	NS		1 > 2
Social characteristic							
Incarceration before 15	1.55 (1.16–2.07)**	0.038	NS		1.56 (1.37–1.78)***	0.047	1, 2 < 3
Incarceration after 15	2.15 (1.74–2.66)***	0.105	NS		2.33 (2.14–2.53)***	0.144	1, 2 > 3
PY police trouble	NS		NS		1.84 (1.51–2.25)***	0.043	2 > 3
Violence	1.73 (1.62–1.84)***	0.251	1.15 (1.10–1.20)***	0.108	1.75 (1.70–1.80)***	0.316	1 > 2 > 3
PY homelessness	2.87 (2.01–4.09)***	0.067	1.70 (1.31–2.20)***	0.056	NS		1 > 2, 3
Parent drug problem	1.55 (1.21–1.97)***	0.050	1.39 (1.15–1.68)***	0.057	NS		1 > 2, 3
Parent alcohol problem	1.51 (1.27–1.81)***	0.090	NS		NS		1 > 3
Parent suicide attempt	2.03 (1.53–2.71)***	0.062	1.75 (1.39–2.20)***	0.071	NS		1 > 2, 3
Childhood neglect	1.02 (1.01–1.04)***	0.065	1.02 (1.01–1.03)***	0.075	NS		1 > 2, 3
Childhood sexual abuse	1.09 (1.06–1.11)***	0.079	1.09 (1.07–1.11)***	0.117	NS		1 > 2, 3
Any trauma	2.04 (1.67–2.48)***	0.194	NS		NS		1 > 3
Any discrimination	1.33 (1.11–1.59)**	0.062	NS		NS		1 > 3
Religious service > 1 per month	0.67 (0.56–0.79)***	–0.112	NS		NS		1 < 3
Total 2 week social contacts	NS		0.99 (0.98–0.99)***	–0.097	NS		1 > 2
MHRQOL	0.97 (0.96–0.97)***	–0.193	0.98 (0.97–0.98)***	–0.155	NS		1 < 2, 3
Clinical characteristic							
PY single psychiatric diagnosis	3.36 (2.75–4.11)***	0.214	NS		NS		1 > 3
PY > 1 psychiatric diagnosis	6.33 (5.10–7.84)***	0.243	2.32 (1.97–2.72)***	0.172	NS		1 > 2, 3
PY > 1 SUD diagnosis	NS		1.36 (1.09–1.69)**	0.044	NS		1 > 2
Medical comorbidities	1.12 (1.06–1.19)***	0.073	1.12 (1.06–1.17)***	0.074	NS		1 > 2, 3

Group 1: Those with lifetime suicide attempt and SUD

Group 2: Those with lifetime suicide attempt or SUD

Group 3: Those without lifetime suicide attempt and SUD

MHRQOL mental health related quality of life, *NS* non-significant, *OR* odds ratio, *PY* past year, *SRC* standard regression coefficient, *SUD* substance use disorder

*All or significant = $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

jobs for less educated US adults, leading to social and economic decline in many communities, less chances for marriage, and loss of opportunities for meaningful work [1–3], all of which were observed in our study, to varying degrees,

among those with lifetime SUD and suicide attempts. Case and Deaton specifically highlight White race and the lack of a bachelor's degree as risk factors in their analysis [1–3] and we too found the proportion of those who were White as well

Table 5 Stepwise, multivariable-adjusted logistic regression analysis of mental health service use differentiating the three groups

Groups	Lifetime mental health treatment ($N=9573$; 26.5%) OR (95% CI)	Lifetime substance use treatment ($N=3036$; 8.4%) OR (95% CI)	Lifetime psychiatric treatment ($N=7877$; 21.8%) OR (95% CI)	Lifetime self- help group ($N=2751$; 7.8%) OR (95% CI)	Consulted clergy for SUD lifetime ($N=2676$; 7.6%) OR (95% CI)
Lifetime suicide attempt or SUD	2.98 (2.68–3.31)*	1.95 (1.45–2.62)*	2.77 (2.29–3.35)*	3.03 (2.67–3.43)*	2.16 (1.59–2.94)*
Lifetime suicide attempt and SUD	5.62 (4.49–7.02)*	2.74 (1.94–3.87)*	6.06 (4.62–7.94)*	4.37 (3.61–5.28)*	2.68 (1.89–3.81)*

Reference group is those with no lifetime SUD and suicide attempt
Controlling for all factors differentiating the three groups of interest
CI confidence interval, *OR* odds ratio, *SUD* substance use disorder
* $p < 0.001$

as without a bachelor's degree to be highest among those living with both SUD and suicide attempt. Another observation of Case and Deaton, that fewer adults are now affiliated with a religious group [3], was also found especially among those living with both lifetime SUD and suicide attempts.

While Case and Deaton argue that the high cost of health care in the US is a key factor of “deaths of despair” and a strong driving force of the increased mortality rate [3], our analysis showed there was little differences between groups in having any insurance coverage although those living with both conditions were less likely to be covered by private insurance, twice as likely as others to be covered by Medicaid, and much more likely to report receipt of mental health services.

Although our study is largely consistent with Case and Deaton's work in that White race and socioeconomic adversities are more common in those living “lives of despair,” we identified deeper multi-generational roots of their sufferings in both parental and their own childhood experiences, and a plethora of psychiatric disorders including depressive disorders. Previous studies have linked childhood trauma as a strong risk factor for suicidal behavior [40, 41], as well as psychiatric disorders including depressive disorders and SUD [42, 43]. As one might expect, those who experienced ACEs have been reported previously, as found here, to have more severe, treatment resistant psychiatric problems [44–46]. Previous research has also strongly suggested that a family history of either suicide or SUD is one of the most potent risk factors for either future suicidal behavior [47] or SUD [48].

In the multivariate model, one of the strongest predictors that differentiated those living with both SUD and suicide attempt was having one or more psychiatric diagnoses. This too is consistent with studies reporting that psychiatric

disorders highly co-occur with SUD [49] and are strong risk factors of both suicidal behavior [50, 51] and overdose [52]. In sum, from a clinical point of view, while acknowledging the socioenvironmental factors contributing to “deaths of despair,” we have uncovered critical intercorrelated background factors to “lives of despair” that lie deep in family histories of behavioral problems which may underpin or exacerbate vulnerability to socio-economic changes in the US.

Paralleling the findings on the prevalence of psychiatric disorders, most of those with both conditions reported had received mental health treatment in their lifetime, far more than those with either one or neither condition. This trend was observed across several different measures of professional and informal service use, and was even more pronounced after controlling for other potentially confounding factors. However, despite this trend in service use, the indexes of current quality of life (e.g., MCS, PCS, and EQ-5D) for those who had both conditions were far worse than those with either or neither, whereas the differences in the other two groups were less pronounced. There was no difference in receipt of any insurance coverage; however, those with both conditions were twice as likely to be covered by Medicaid. This trend may have become even more pronounced in recent years given that the Affordable Care Act came into effect in 2014, immediately after NESARC-III was conducted. A recent study found that while the differences in quality of care between Medicaid and private insurance was modest, Medicaid was associated with fewer office visits and prescriptions and more ED visits compared to private insurance, possibly due to limited access to outpatient care in Medicaid [53]. It is possible that although adults with multiple conditions utilize mental health treatment more than others, the treatment they receive may not

be of high quality or adequate to meet their needs and make major changes in their lives.

Although the work of Case and Deaton was the starting point of this study, it needs to be situated within a growing literature on the adverse effects of behavioral multimorbidity, more generally [16, 17], the recent recognition of suicidal aspects of SUD [9, 10, 54], and the growing attention to the social determinants of mental health [55–57]. It is also important to note that there have been studies disputing the validity of Case and Deaton's observations [58–61]. For example, a previous study using official US mortality data showed that while the relative contribution to overall mortality rates from drug-related deaths has increased dramatically between 1980 and 2014, the contributions from alcohol-related and suicide deaths remained stable [58]. The same group has shown that “deaths of despair” have risen equally for non-Hispanic Whites and non-Hispanic Blacks, and this trend is overwhelmingly driven by period-based increases in drug-related deaths due to the opioid epidemic [59]. Further, another study criticized Case and Deaton's work suggesting that changes in economic conditions accounted for less than one-tenth of the rise in drug-related mortality rates, and concluded that “deaths of despair” is a mere manifestation of increasing “drug problems” [61]. Rather than a syndrome specifically related to SUD and suicidality, our findings point to a complex tapestry of multiple, interacting, mental health, behavioral and socio-economic factors which escape simple mono-causal explanation or remedy, but which deserve increasing multidisciplinary study and intervention both at the level of clinical practice and social policy.

Our study has several limitations. First and foremost, the study examined lifetime SUD and suicide attempt instead of more proximal measures of SUD and suicide attempt (e.g., past-year measures) which may more accurately capture those at highest risk for “lives of despair.” Second, related to our first limitation, given that those who died from SUD and suicide are not represented in this study, it is impossible to infer that the results of this study are generalizable to people who died from these conditions. Third, as a cross-sectional study from a single point in time, it does not address if trajectories of many concomitant problems accompanying the combination of lifetime SUD and suicide attempts have become more prevalent in recent decades or whether any one problem has played a leading role over any other. Fourth, mental health service utilization was measured grossly and does not adequately address the extent of service use (i.e., frequency, intensity, or long-term use), its quality or reliance on effective evidence-based treatments. Fifth, given the nature of the survey relying on self-report, it is possible that the prevalence captured for both past suicide attempts and SUD may in fact be underestimated due to social desirability bias [62]. Sixth, although NESARC-III was conducted

during the period studied by Case and Deaton, the SUD landscape has changed since 2012–2013 with the increase of fentanyl [63] which is another reason why our findings on the magnitude of “lives of despair” maybe an underestimation for the current climate. Seventh, our multivariate model is exploratory at best and causal interpretations cannot be made. Further studies with longitudinal data and more robust research designs are needed to confirm our findings. Lastly, the actual mortality rate of individuals who have both conditions in this study is unknown.

Notwithstanding these limitations, this study provides a snapshot, in a nationally representative sample, of a subgroup of US adults who may be at high risk for “deaths of despair” and many other problems. The sociodemographic/economic and behavioral characteristics emphasized by Case and Deaton have mostly emerged in our results as well. From a clinical point of view, our results show that the problems of US adults living “lives of despair” are deeply rooted in individual life histories and more closely related to their childhood and parental adverse experiences, and psychiatric multimorbidity as well as to socio-economic hard times. These results suggest that mental health treatment by itself may not be enough to solve these sufferings, and likely require interdisciplinary interventions involving social policy reforms, socioeconomic interventions and mental health treatment in effective combinations in need of being both designed and tested.

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Declarations

Conflicts of interest All authors report no competing interests.

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