



Research paper

Socioeconomic status, alcohol use disorders, and depression: A population-based study

Aurélie M. Lasserre^{a,b,*}, Sameer Imtiaz^a, Michael Roerecke^{a,c,d}, Markus Heilig^e,
Charlotte Probst^{a,f,g}, Jürgen Rehm^{a,c,d,g,h,i,j,k}

^a Institute for Mental Health Policy Research, Centre for Addiction and Mental Health (CAMH), 33 Ursula Franklin Street, Toronto, ON M5S 2S1, Canada

^b Addiction Medicine, Department of Psychiatry, Lausanne University Hospital, Rue du Bugnon 23, 1011 Lausanne, Switzerland

^c Dalla Lana School of Public Health, University of Toronto, 155 College Street, Toronto, ON M5T 1P8, Canada

^d Campbell Family Mental Health Research Institute, CAMH, 33 Ursula Franklin Street, Toronto, ON M5S 2S1, Canada

^e Center for Social and Affective Neuroscience, Linköping University, SE-581 83 Linköping, Sweden

^f Heidelberg Institute of Global Health, Heidelberg University, Im Neuenheimer Feld 130.3, 69120 Heidelberg, Germany

^g Department of Psychiatry, University of Toronto, 250 College Street, Toronto, ON M5T 1R8, Canada

^h Institute of Clinical Psychology and Psychotherapy & Center of Clinical Epidemiology and Longitudinal Studies, Technische Universität Dresden, Chemnitz Str. 46, 01187 Dresden, Germany

ⁱ Department of International Health Projects, Institute for Leadership and Health Management, I.M. Sechenov First Moscow State Medical University, Trubetskaya str., 8, b. 2, 119992, Moscow, Russian Federation

^j Agència de Salut Pública de Catalunya, 81-95 Roc Boronat St., 08005 Barcelona, Spain

^k Center for Interdisciplinary Addiction Research, Department of Psychiatry and Psychotherapy, University Medical Center Hamburg-Eppendorf, Martinistraße 52, 20246 Hamburg, Germany



ARTICLE INFO

Keywords:

Educational attainment

Alcohol consumption

Depressive disorders

Severity of mental disorders

Interaction

Cohort

General population

ABSTRACT

Background: Depressive disorders (DD) and alcohol use disorders (AUD) frequently co-occur. They are key to understanding the current increases in “deaths of despair” among individuals with lower socioeconomic status (SES). The aim of this study was to assess the prospective bidirectional associations between AUD and DD, as well as the effect of SES on these two conditions.

Methods: The National Epidemiologic Survey on Alcohol and Related Conditions is a cohort study representative of the US adult population, which began in 2001–2002, with follow-up interviews conducted 3 years later. SES was primarily operationalized as educational attainment. AUD, DD, and their levels of severity were defined according to the DSM-5 criteria.

Results: The risk of developing an incident DD increased gradually with the recency and the severity of AUD at baseline, but the converse was not observed. Lower SES was an independent risk for incident AUD or DD. SES did not modify the prospective association between AUD and DD.

Limitations: The absence of interaction between SES and moderate or severe AUD for the incident DD must be considered with caution due to the limited number of DD cases reported in these AUD categories.

Conclusions: This result is consistent with a causal relationship between AUD and DD, and suggests that therapeutic interventions for AUD may also have beneficial effects to lower DD rates. The independent effects of a lower SES and AUD on DD may result in a vulnerable population cumulating disorders with heavy consequences on health and social well-being.

1. Introduction

In many societies, including in the United States (US), depressive disorders (DD) and alcohol use disorders (AUD) are among the most prevalent psychiatric disorders (Substance Abuse and Mental Health

Services Administration, 2019). Among US adults, 14.0 million qualified for an AUD in 2019 (SAMHSA Center for Behavioral Health Statistics and Quality, 2019) and more than 17.3 million experienced at least one depressive episode in 2017 (National Institutes of Mental Health, 2017). In addition, these disorders can co-occur; the presence of either disorder

* Corresponding author at: Addiction Medicine, Department of Psychiatry, Lausanne University Hospital, Rue du Bugnon 23, 1011 Lausanne, Switzerland.

E-mail address: aurelie.lasserre@chuv.ch (A.M. Lasserre).

<https://doi.org/10.1016/j.jad.2021.12.132>

Received 8 September 2021; Received in revised form 17 December 2021; Accepted 31 December 2021

Available online 2 January 2022

0165-0327/© 2022 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

doubles the risk of the other disorder (Boden and Fergusson, 2011). Furthermore, this co-occurrence can be characterized by greater severity and worse prognosis than either disorder alone (Greenfield et al., 1998; Hasin et al., 2002), including a heightened risk for suicidal behavior (Conner et al., 2014). Three main hypotheses have been made to explain this comorbidity. First, a causal relationship between AUD and DD has been proposed, according to which alcohol use could lead to depression through changes in metabolism, neurotransmitter function, or through the consequences of AUD on social life (Fergusson et al., 2009; Li et al., 2020). Second, DD might increase alcohol consumption as a coping mechanism, which can result in AUD when increased use persists over time. This is known as the self-medication hypothesis (Abraham and Fava, 1999; Turner et al., 2018). Third, an overlapping genetic vulnerability or environmental risk factors, such as adverse childhood events or other traumatic experiences, may contribute to the co-occurrence of these two conditions (Capusan et al., 2021; Caspi et al., 2014; Gilbert et al., 2015).

Both these disorders affect more socially disadvantaged people (Bellis et al., 2016; Hall, 2017; Haugland et al., 2015; Melchior et al., 2013). Thus, both DD and AUD are key to understanding the current phenomenon of “deaths of despair” in the US, where overall decreases in life expectancy, even before the COVID-19 pandemic, have been characterized by increases in poisoning, alcoholic liver cirrhosis, and suicides (Case and Deaton, 2015, 2017; Case and Deaton, 2020), especially among the two-thirds of Americans without a college degree (Case and Deaton, 2021; Sasson and Hayward, 2019). Education is a key indicator of socioeconomic status (SES), as people with low education in the US are increasingly being left behind with fewer prospects for secure, financially stable employment (Hummer and Lariscy, 2011; Walsemann et al., 2013).

Longitudinal observational studies assessing a direction in a potential causality between AUD and DD are still scarce and have shown conflicting results (Boden and Fergusson, 2011; Conner et al., 2014; Kohler et al., 2018). Moreover, AUD and DD are both known to cover heterogeneous clinical presentations with a wide continuum, ranging from moderate and brief disorders to severe disorders with devastating life consequences. In that regard, taking their respective severity into account, as suggested in the DSM-5, might be a key factor in the understanding of a potential causal association between AUD and DD (Graham et al., 2007; McHugh and Weiss, 2019; Paris, 2014; Rehm et al., 2017). Finally, to our knowledge, whether SES modifies this longitudinal bidirectional association has not been studied. Accordingly, using data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a large nationally representative survey with a follow-up component (Grant and Dawson, 2021; Hasin and Grant, 2015), the aims of the present study were to: 1. explore the relative strength of a prospective bidirectional association between AUD and DD, taking their respective severity into account, in order to distinguish a potential causal direction, 2. examine if a low SES prospectively independently increases the risks of developing an AUD or a DD, and 3. assess whether the association between AUD and DD changes according to the SES (i.e., assess a potential interaction between SES and each disorder for incidence of the other disorder).

2. Methods

2.1. Participants

The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) Wave 1 and Wave 2 was a longitudinal survey, designed under the National Institute on Alcohol Abuse and Alcoholism (NIAAA)'s direction to determine the magnitude of AUDs and their associated disabilities in the general adult population. The NESARC sample represents the civilian, noninstitutionalized adult (18 years old or more) population of the US, including people living in households, military personnel living off base, and people residing in group quarters.

The three-stage sampling frame for the NESARC was based on the Census 2000/2001 Supplementary Survey (C2SS). For Wave 1, data were collected during 2001–2002 in face-to-face interviews ($N = 43,093$), and for Wave 2, 34,653 respondents were re-interviewed during 2004–2005. Of the 8440 Wave 1 respondents who were not included in Wave 2, 3134 were not eligible for a Wave 2 interview because they were institutionalized, mentally/physically impaired, on active duty in the armed forces throughout the Wave 2 interview period, deceased, or had been deported. The remaining respondents ($N = 5306$) refused to participate or could not be reached or located. The cumulative survey response rate was 70.2%.

Participants who had ever presented with a manic or hypomanic episode at Wave 1 were excluded from all analyses. For analyses regarding the incidence of DD between Wave 1 and 2, participants with a lifetime DD at Wave 1 were also excluded. Similarly, for analyses regarding the incidence of AUD between Wave 1 and 2, participants with a lifetime AUD at Wave 1 were excluded.

2.2. Measures

NESARC's diagnostic classifications were based on the Alcohol Use Disorder and Associated Disability Interview Schedule–DSM-IV Version (AUDADIS-IV), a fully structured, computer-assisted diagnostic interview (Grant et al., 2003). NESARC contained questions that operationalized the criteria set forth in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) for alcohol and drug use disorders and mood disorders (major depressive disorder, bipolar I and bipolar II disorders, dysthymia, and hypomania).

For the present study, the definition of AUD was based on the DSM-5 (American Psychiatric Association, 2013), excluding the craving criteria which was not assessed in the Wave 1 and 2 NESARC interviews. Accordingly, alcohol use and AUD at Wave 1 were split into the following six categories: lifetime abstinence (reference), drinkers (past or current) without AUD, remitted AUD (occurred prior to the last 12 months), mild AUD (2–3 symptoms), moderate AUD (4–5 symptoms) or severe AUD (6 or more symptoms). Mild, moderate, or severe AUD referred to symptoms present during the last 12 months. We used the DSM-5 definition of DD as well, which includes major depressive disorders and persistent depressive disorder (former chronic major depressive disorder and dysthymia). DD at Wave 1 were also categorized according to their temporality and severity. Remitted DD had occurred prior to the last 12 months. The current DD, which had occurred in the last 12 months, were categorized according to their severity, based on the number of criterion symptoms. We used the DSM-5 specifier to determine the current severity of the DD. Mild included the DD with 0 to 1 symptom in excess of those required to make the diagnosis, moderate included the DD with 2 to 3 symptoms in excess, and severe included the DD fulfilling all the criterion symptoms. If both major depressive disorder and persistent depressive disorder were present, we chose the category with the higher severity.

SES was primarily defined according to the education attainment, and for sensitivity analyses, household income was used (Galobardes et al., 2006). Education was split into having a high school diploma or less (low), some college but no bachelor's degree (medium), and a bachelor's degree or more (high) (Case and Deaton, 2020). The 2001 poverty guidelines of the Department of Health and Human Services, which take into consideration the number of people living in the household and its combined income, were used to categorize the income into low (below the poverty threshold), medium (above the poverty threshold and under four times the poverty threshold), and high (above four times the poverty threshold) (Department of Health and Human Services, 2020).

The race and ethnicity variable was constructed from the Hispanic origin variable and the single classification race recode according to an algorithm developed by the Census Bureau (Wave 1 NESARC Data

Notes. Bethesda, MD: NIAAA, 2004). Individuals who reported being of Hispanic origin were coded as having a Hispanic ethnicity, regardless of their race. Non-Hispanic individuals who reported multiple races were coded into a single category in the following order of priority: 1) Black, 2) American Indian/Alaska Native, 3) Asian/Native Hawaiian/Pacific Islander, 4) White.

2.3. Statistical analyses

The NESARC sample was weighted to adjust for non-response at the household and person levels, the selection of one person per household, and oversampling of young adults, Hispanics, and Blacks. We used multiple logistic regression models to assess the prospective associations between SES, DD, and AUD. Effect modification by SES was investigated on multiplicative and additive scales, following the approach described by [Knol and VanderWeele \(2012\)](#). Model-adjusted risks, model-adjusted risk differences, and additive interaction tests were computed using the predictive margin functions PREDMARG and PRED_EFF in SUDAAN. Here, predicted marginal prevalences of each outcome were generated using the specified logistic regression models, and group comparisons were performed through contrast statements ([Sarvet and Wall, 2016](#)). We used the Stata 17 ([StataCorp, 2021](#)) and SUDAAN ([Research Triangle Institute, 2018](#)) softwares. The latter uses Taylor series linearisation in variance estimation to make adjustments for the sampling methodology.

2.4. Ethical statement

All participants gave informed consent to participate. The research protocol received full ethical review and approval from the U.S. Census Bureau and the U.S. Office of Management and Budget.

3. Results

3.1. SES and AUD as predictors of DD during the follow-up period

After exclusions of participants who already had a manic or hypomanic episode or a DD at baseline, 27,571 participants remained in the analyses (49.5% female, mean age 45.9 years). Overall, 6.4% developed a DD in the 3 years leading up to the follow-up interview. Compared to lifetime abstainers, the risk for developing a DD during the 3 years prior to follow-up increased gradually among non-abstainer participants according to the severity and the recency of their AUD at baseline (OR, 95% CI: 1.20, 1.01–1.41; 1.28, 1.04–1.57; 1.68, 1.22–2.32; 1.92, 1.31–2.81 and 2.35, 1.07–5.14 for participants without; with remitted; mild; moderate and severe AUD, respectively). Regarding SES, a medium or low level of education were independent risk factors for developing a DD, compared to a high level of education (OR, 95% CI: 1.35, 1.15–1.58 and 1.52, 1.27–1.81, respectively) ([Table 1](#)). Sensitivity analysis using household income as an SES indicator showed similar results ([Supplementary material, Table 1–1](#)). Stratified analyses by sex followed the same trends for males and females ([Supplementary material, Table 1–2](#)). SES did not modify the association between AUD and DD; comparing the high versus the low SES, we found no interaction between SES and AUD on a multiplicative, nor on an additive scale ([Supplementary material, Table 1–3](#)).

3.2. SES and DD as predictors of AUD during the follow-up period

After exclusions of participants who already had a manic or hypomanic episode or an AUD at baseline, 22,066 participants remained in the analyses (59.8% female, mean age 47.2 years). Overall, 7.0% developed an AUD during the follow-up period. The risk for developing an AUD during the 3 years of follow-up did not differ according to DD diagnosis, but was increased by a medium or a low level of education at baseline OR, 95% CI: 1.38, 1.11–1.70 and 1.27, 1.00–1.61, respectively ([Table 2](#)). This was not confirmed in the sensitivity analysis using

Table 1

Incidence of depressive disorders (DD) between Waves 1 and 2, according to alcohol use disorders (AUD) categories and socioeconomic status (SES) at Wave 1.

	N	% (SE)	N with DD	% (SE)	OR (95% CI)
AUD categories					
Lifetime abstainer	5420	18.2 (0.7)	381	17.3 (1.5)	1 (ref.)
Drinker without AUD	14,061	50.8 (0.6)	905	50.5 (1.6)	1.20 (1.01–1.41)
Remitted AUD	6123	23.3 (0.6)	384	21.0 (1.4)	1.28 (1.04–1.57)
Mild AUD	1355	5.2 (0.2)	104	6.9 (0.9)	1.68 (1.22–2.32)
Moderate AUD	412	1.7 (0.1)	43	2.7 (0.4)	1.92 (1.31–2.81)
Severe AUD	200	0.9 (0.1)	22	1.6 (0.6)	2.35 (1.07–5.14)
SES (educational attainment)					
High	6817	26.0 (0.7)	359	19.6 (1.3)	1 (ref.)
Medium	8988	33.1 (0.4)	631	35.4 (1.2)	1.35 (1.15–1.58)
Low	11,766	40.9 (0.6)	849	45.0 (1.5)	1.52 (1.27–1.81)
Sex					
Male	12,260	50.5 (0.4)	546	35.2 (1.5)	1 (ref.)
Female	15,311	49.5 (0.4)	1293	64.8 (1.5)	2.15 (1.89–2.45)
Age [Mean (SE)]					
	27,571	45.9 (0.2)	1839	41.9 (0.5)	0.99 (0.98–0.99)
Race/ethnicity					
White	15,611	69.7 (1.6)	968	66.2 (2.2)	1 (ref.)
Black	5511	11.6 (0.7)	367	11.8 (1.0)	0.96 (0.82–1.13)
AI/AN	397	1.9 (0.2)	43	3.3 (0.6)	1.82 (1.27–2.61)
Asian/NH/PI	834	4.6 (0.5)	45	3.8 (0.9)	0.89 (0.59–1.35)
Hispanic	5218	12.2 (1.3)	416	15.0 (1.7)	1.15 (0.97–1.36)

AI/AN:American Indian/Alaska Native, NH/PI:Native Hawaiian/Pacific Islander.

household income as SES indicator ([Supplementary material, Table 2-1](#)). The stratified analyses by sex gave similar results among males and females ([Supplementary material, Table 2-2](#)). There was no interaction between SES and DD on a multiplicative, nor on an additive scale.

4. Discussion

This prospective study, with participants being representative of the US population, shows that AUD severity plays a key role in the risk of developing a DD, with a dose-response association, and that a remitted AUD remains a risk factor for developing a DD. These results provide consistent evidence with a unidirectional causal relationship between AUD and subsequent DD. Moreover, we found that a low SES was an independent risk factor for incident DD and for incident AUD, and that the strength of the association between AUD and DD did not vary between low or high SES. Our results are consistent with a meta-analysis of ten cross-sectional and longitudinal studies which supported the hypothesis of AUD as a precursor of DD ([Boden and Fergusson, 2011](#)), as well as with a recent large genomic study ([Grotzinger et al., 2020](#)) which showed a causal association between problematic alcohol use and depression using Mendelian randomization. Examining the older adults

Table 2

Incidence of alcohol use disorders (AUD) between Waves 1 and 2, according to depressive disorders (DD) categories and socioeconomic status (SES) at Wave 1.

	N	% (SE)	N with AUD	% (SE)	OR (95% CI)
DD categories					
Never had DD	19,373	88.5 (0.3)	1289	88.8 (1.2)	1 (ref.)
Remitted DD	1554	6.8 (0.2)	90	5.7 (0.7)	1.01 (0.76–1.35)
Mild DD	271	1.2 (0.1)	15	1.0 (0.3)	0.66 (0.34–1.30)
Moderate DD	540	2.2 (0.1)	44	2.6 (0.5)	1.17 (0.77–1.77)
Severe DD	328	1.4 (0.1)	22	1.9 (0.5)	1.39 (0.85–2.28)
SES (educational attainment)					
High	5110	24.5 (0.7)	246	18.3 (1.8)	1 (ref.)
Medium	6974	32.2 (0.5)	563	39.5 (1.6)	1.38 (1.11–1.70)
Low	9982	43.3 (0.6)	651	42.2 (1.9)	1.27 (1.00–1.61)
Sex					
Male	7592	40.2 (0.5)	779	58.6 (1.5)	1 (ref.)
Female	14,474	59.8 (0.5)	681	41.4 (1.5)	0.47 (0.41–0.54)
Age [Mean]	22,066	47.2 (0.2)	1460	33.2 (0.5)	0.94 (0.94–0.95)
Race/ethnicity					
White	11,872	67.2 (1.8)	742	63.7 (2.2)	1 (ref.)
Black	4638	12.4 (0.8)	331	14.8 (1.3)	0.94 (0.78–1.13)
AI/AN	300	1.8 (0.2)	23	2.2 (0.6)	1.32 (0.73–2.42)
Asian/NH/PI	760	5.5 (0.6)	32	3.8 (1.1)	0.53 (0.31–0.91)
Hispanic	4496	13.1 (1.4)	332	15.4 (1.8)	0.75 (0.63–0.90)

AI/AN:American Indian/Alaska Native, NH/PI:Native Hawaiian/Pacific Islander.

(60 years old or more) of the same NESARC sample, [Chou et al. \(2011\)](#) did not find any prospective association between AUD and major depressive disorder, in either direction. This might be explained by a decreasing risk of DD with age and by the manner in which the two disorders were measured—as being either present or absent—without accounting for their independent severity levels. [Boschloo et al. \(2012\)](#) used the number of AUD symptoms during the past 12 months as the exposure variable and also found a linear dose-response association with incident DD. We found no significant association between DD and the risk of developing an AUD, consistent with most ([Boden and Fergusson, 2011](#); [Fergusson et al., 2009](#)), but not all, prior studies ([Turner et al., 2018](#)). The association between SES and DD is consistent with previous studies showing a social gradient in the incidence of depression ([Grant et al., 2009](#); [Melchior et al., 2013](#)). Consistent with our results, the association between SES and AUD is more widely debated than the one between SES and DD ([Grant et al., 2009](#); [Lund et al., 2018](#)).

Our finding that SES did not modify the association of AUD with DD is unexpected, given the literature on the alcohol harm paradox, according to which people of low SES experience greater alcohol-related harm than those of high SES for the same or lower level of alcohol consumption ([Hall, 2017](#); [Probst et al., 2020, 2014](#)). A meta-analysis of 133 million people compared socioeconomic inequality in

alcohol-attributable and all-cause mortality and found a relative risk of dying from alcohol-attributable causes of 1.7-fold the relative risk of all-cause mortality ([Probst et al., 2014](#)). However, to our knowledge, no study has examined the potential influence of SES on the prospective association between AUD and DD (i.e., the interaction between SES and AUD). Two cross-sectional studies have examined whether SES influenced the association between alcohol use and depressive symptoms and found conflicting results ([Assanangkornchai et al., 2020](#); [Martinez et al., 2015](#)). In a Norwegian sample of more than 10 000 adults, [Martinez et al. \(2015\)](#) found an interaction between employment and depressive symptoms on the risk of heavy episodic drinking, but no interaction between education level and depressive symptoms regarding alcohol use. In a Thai sample of more than 13 000 participants, [Assanangkornchai et al. \(2020\)](#) found an association between major depressive episodes and AUD, which was modified by wealth and education, but not employment status. Patterns of drinking seem to vary across low-, middle-, or high-income countries and cultures and might affect possible interactions with SES ([Gritter et al., 2013](#); [Rehm et al., 2017](#)).

This study has several limitations. First, we could not take craving—which is the only DSM-5 criteria that differs from DSM-IV in the assessment of AUD severity—because it was not assessed in the AUDADIS-IV interview. Craving has been shown to be well correlated with the other DSM criteria, but this symptom is rarely present and does not have much impact on the descriptive epidemiology of AUD ([Keyes et al., 2011](#); [Saha et al., 2006](#)). Thus, missing the craving criteria could have led us to an underestimation of the AUD severity, and consequently of the observed effects, but is not likely to have modified the observed associations. Second, this survey was conducted in the first decade of the 21st century, prior to the decrease in life expectancy due to “deaths of despair”. However, the trends in substance use poisoning, liver cirrhosis deaths, and suicide began before the effect on life expectancy was manifest ([Shiels et al., 2020](#)). Moreover, AUD and DD are often relapsing disorders persisting over long periods of time, leading to an increased mortality after many years ([Carvalho et al., 2019](#); [Gilman et al., 2017](#)). Third, we had no information about adverse childhood events or other traumatic experiences at baseline, which have been associated with both AUD and DD ([Capusan et al., 2021](#); [Caspi et al., 2014](#); [Gilbert et al., 2015](#)). However the nature of the association between adverse childhood events and mental health is still debated and disentangling these complex interrelationships would go beyond the present study ([Danese and Widom, 2021](#)). Fourth, we have not included anxiety disorders or cigarette smoking in our models, despite their possible association with AUD and DD. Considering the high correlations between anxiety disorders and DD, and cigarette smoking and AUD, including such variables in our models would have blurred the observed association with an overadjustment. Moreover, a previous publication on NESARC data among older adults has already shown models of prospective associations, including all measured psychiatric disorders ([Chou et al., 2011](#)). And, finally, our findings of an absence of interaction between SES and moderate or severe AUD for the incidence of DD must be considered with caution due to the small numbers of DD cases reported in these AUD categories.

The major role played by low SES and AUD on the incidence of DD is likely to be multifactorial. The experience of deprivation, especially when compared to other people, and the limited access to health care are likely to adversely affect mental health ([Lund et al., 2018](#)). Low SES also impacts the living conditions and might increase the risk of being confronted by violence. For example, more walkable neighborhoods with leisure opportunities are associated with a reduced prevalence of DD and AUD ([Peen et al., 2010](#)). Regarding AUD, addiction dramatically alters motivational circuits through multiple changes in neurotransmitter function, which could affect mood ([Koob and Volkow, 2016](#)). The direct neurotoxicity of alcohol might also result in an increased risk of DD. The consequences of AUD on multiple aspects of social life, such as a disruption of affective relationships, employment-related difficulties or

legal problems are causes for a deteriorated mood as well (Carvalho et al., 2019). Our results seem to exclude the self-medication hypothesis of DD as a precursor to AUD (Turner et al., 2018). Regarding the hypothesis of a shared genetic susceptibility, which could not be explored within our data, genetic studies on large samples have demonstrated that AUD and DD arise from two distinct genetic factors (Grotzinger et al., 2020; Kendler et al., 2003). Finally, our results moderately support the hypothesis of shared risk factors between AUD and DD, in particular factors related to SES.

The conjugated effect of SES and AUD on DD contribute to the development of a vulnerable population with cumulating disorders with severe consequences on health and social well-being. The deaths of despair (Case and Deaton, 2015, 2017; Case and Deaton, 2020, 2021; Sasson and Hayward, 2019) —a decrease in life expectancy in the US characterized by increases in substance use poisoning, alcohol-related liver mortality, and suicides among the lower socioeconomic stratum—is a striking example of the development of a vulnerable population and its consequences. This shift in life expectancy has been described from a social and economic perspective. However, it is worth noting that the ‘deaths of despair’ are all closely linked to mental health, and particularly to depression. Our results show that depression might have been underestimated as an underlying cause in deaths of despair. Better capturing and measuring “despair” might help mental health specialists to study the deaths of despair as well, which could bring a more thorough understanding of this phenomenon (Shanahan and Copeland, 2021; Shanahan et al., 2019). Moreover, as AUD prevalence has increased in the last decades in the US population, especially among the socioeconomically disadvantaged subgroups of the population (Grant et al., 2017), the observed effects of low SES and AUD on the incidence of DD twenty years ago might even be of more importance today. Studies examining the long-term effects of SES and various degrees of AUD severity on mental health are urgently needed and might help us better understand the “deaths of despair” phenomenon. Adding a mental health perspective to the social and economic perspectives on deaths of despair could help in capturing the complex interconnection of environmental, social, and biological pathways to the current increase in suicide, drug- and alcohol-related mortality rates. Targeting the lower SES groups of the population in AUD prevention strategies might help reduce these disparities in mental health and have a beneficial effect on the incidence of depression as well.

Funding

This work was supported by the Swiss National Science Foundation (Grant Number P2LAP3_191273) and by the National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health (grant number 1R01AA028009). The content is solely the responsibility of the authors and does not necessarily represent the official views of the Swiss National Science Foundation and National Institutes of Health.

CRedit authorship contribution statement

Aurélie M. Lasserre: Conceptualization, Formal analysis, Methodology, Writing – review & editing. **Sameer Intiaz:** Formal analysis, Methodology, Writing – review & editing. **Michael Roerecke:** Conceptualization, Methodology, Writing – review & editing. **Markus Heilig:** Methodology, Writing – review & editing. **Charlotte Probst:** Methodology, Writing – review & editing. **Jürgen Rehm:** Conceptualization, Methodology, Writing – review & editing.

Declarations of Competing Interest

All other authors declare that they have no conflicts of interest.

Acknowledgments

The National Institute on Alcohol Abuse and Alcoholism, as part of the US National Institutes of Health, conducted and sponsored the first and second waves of the NESARC, the data from which were made freely available. We would like to thank Astrid Otto (CAMH) for the scientific editing of this article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jad.2021.12.132.

References

- Abraham, H.D., Fava, M., 1999. Order of onset of substance abuse and depression in a sample of depressed outpatients. *Compr. Psychiatry* 40, 44–50.
- American Psychiatric Association, 2013. *Diagnostic and Statistical Manual of Mental disorders: DSM-5*, 5th ed. VA: American Psychiatric Association, Arlington. [2013].
- Assanangkornchai, S., Nontarak, J., Aekplakorn, W., Chariyalertsak, S., Kessomboon, P., Taneepanichkul, S., 2020. Socio-economic inequalities in the association between alcohol use disorder and depressive disorder among Thai adults: a population-based study. *BMC Psychiatry* 20, 553.
- Bellis, M.A., Hughes, K., Nicholls, J., Sheron, N., Gilmore, I., Jones, L., 2016. The alcohol harm paradox: using a national survey to explore how alcohol may disproportionately impact health in deprived individuals. *BMC Public Health* 16, 111.
- Boden, J.M., Fergusson, D.M., 2011. Alcohol and depression. *Addiction* 106, 906–914.
- Boschloo, L., van den Brink, W., Penninx, B.W., Wall, M.M., Hasin, D.S., 2012. Alcohol-use disorder severity predicts first-incidence of depressive disorders. *Psychol. Med.* 42, 695–703.
- Capusan, A.J., Gustafsson, P.A., Kuja-Halkola, R., Igelström, K., Mayo, L.M., Heilig, M., 2021. Re-examining the link between childhood maltreatment and substance use disorder: a prospective, genetically informative study. *Mol. Psychiatry* 26 (7), 3201–3209. <https://doi.org/10.1038/s41380-021-01071-8>.
- Carvalho, A.F., Heilig, M., Perez, A., Probst, C., Rehm, J., 2019. Alcohol use disorders. *Lancet* 394, 781–792.
- Case, A., Deaton, A., 2015. Rising morbidity and mortality in midlife among white non-hispanic Americans in the 21st century. In: *Proceeding of the National Academy Sciences USA*, 112, pp. 15078–15083.
- Case, A., Deaton, A., 2017. Mortality and morbidity in the 21(st) century. *Brook. Pap. Econ. Act.* 397–476, 2017.
- Case, A., Deaton, A., 2020. *Deaths of Despair and the Future of Capitalism*. Princeton University Press, Princeton, NJ.
- Case, A., Deaton, A., 2021. Life expectancy in adulthood is falling for those without a BA degree, but as educational gaps have widened, racial gaps have narrowed. In: *Proceeding of the National Academy Sciences USA*, p. 118.
- Caspi, A., Houts, R.M., Belsky, D.W., Goldman-Mellor, S.J., Harrington, H., Israel, S., Meier, M.H., Ramrakha, S., Shalev, I., Poulton, R., Moffitt, T.E., 2014. The p Factor: one general psychopathology factor in the structure of psychiatric disorders? *Clin. Psychol. Sci.* 2, 119–137.
- Chou, K.L., Mackenzie, C.S., Liang, K., Sareen, J., 2011. Three-year incidence and predictors of first-onset of DSM-IV mood, anxiety, and substance use disorders in older adults: results from Wave 2 of the national epidemiologic survey on alcohol and related conditions. *J. Clin. Psychiatry* 72, 144–155.
- Conner, K.R., Gamble, S.A., Bagge, C.L., He, H., Swogger, M.T., Watts, A., Houston, R.J., 2014. Substance-induced depression and independent depression in proximal risk for suicidal behavior. *J. Stud. Alcohol Drugs* 75, 567–572.
- Danese, A., Widom, C.S., 2021. The subjective experience of childhood maltreatment in psychopathology. *JAMA Psychiatry*.
- Department of Health and Human Services, 2001 poverty guidelines. <https://aspe.hhs.gov/2001-hhs-poverty-guidelines> (accessed 20/11/ 2020).
- Fergusson, D.M., Boden, J.M., Horwood, L.J., 2009. Tests of causal links between alcohol abuse or dependence and major depression. *Arch. Gen. Psychiatry* 66, 260–266.
- Galobardes, B., Shaw, M., Lawlor, D.A., Lynch, J.W., Davey Smith, G., 2006. Indicators of socioeconomic position (part 1). *J. Epidemiol. Commun. Health* 60, 7–12.
- Gilbert, L.K., Breiding, M.J., Merrick, M.T., Thompson, W.W., Ford, D.C., Dhingra, S.S., Parks, S.E., 2015. Childhood adversity and adult chronic disease: an update from ten states and the district of Columbia, 2010. *Am. J. Prev. Med.* 48, 345–349.
- Gilman, S.E., Sucha, E., Kingsbury, M., Horton, N.J., Murphy, J.M., Colman, I., 2017. Depression and mortality in a longitudinal study: 1952–2011. *CMAJ* 189, E1304–e1310.
- Graham, K., Massak, A., Demers, A., Rehm, J., 2007. Does the association between alcohol consumption and depression depend on how they are measured? *Alcohol. Clin. Exp. Res.* 31, 78–88.
- Grant, B.F., Chou, S.P., Saha, T.D., Pickering, R.P., Kerridge, B.T., Ruan, W.J., Huang, B., Jung, J., Zhang, H., Fan, A., Hasin, D.S., 2017. Prevalence of 12-month alcohol use, high-risk drinking, and DSM-IV alcohol use disorder in the United States, 2001–2002 to 2012–2013: results from the national epidemiologic survey on alcohol and related conditions. *JAMA Psychiatry* 74, 911–923.

- Grant, B.F., Dawson, D.A., 2021. Introduction to the national epidemiologic survey on alcohol and related conditions. <https://pubs.niaaa.nih.gov/publications/arih29-2/74-78.htm> (accessed 07/03/2021).
- Grant, B.F., Dawson, D.A., Stinson, F.S., Chou, P.S., Kay, W., Pickering, R., 2003. The alcohol use disorder and associated disabilities interview schedule-IV (AUDADIS-IV): reliability of alcohol consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. *Drug Alcohol Depend.* 71, 7–16.
- Grant, B.F., Goldstein, R.B., Chou, S.P., Huang, B., Stinson, F.S., Dawson, D.A., Saha, T.D., Smith, S.M., Pulay, A.J., Pickering, R.P., Ruan, W.J., Compton, W.M., 2009. Sociodemographic and psychopathologic predictors of first incidence of DSM-IV substance use, mood and anxiety disorders: results from the wave 2 national epidemiologic survey on alcohol and related conditions. *Mol. Psychiatry* 14, 1051–1066.
- Greenfield, S.F., Weiss, R.D., Muenz, L.R., Vagge, L.M., Kelly, J.F., Bello, L.R., Michael, J., 1998. The effect of depression on return to drinking: a prospective study. *Arch. Gen. Psychiatry* 55, 259–265.
- Gritner, U., Kuntsche, S., Gmel, G., Bloomfield, K., 2013. Alcohol consumption and social inequality at the individual and country levels—results from an international study. *Eur. J. Public Health* 23, 332–339.
- Grotzinger, A.D., Mallard, T.T., Akingbuwa, W.A., Ip, H.F., Adams, M.J., Lewis, C.M., McIntosh, A.M., Grove, J., Dalsgaard, S., Lesch, K.P., Strom, N., Meier, S.M., Mattheisen, M., Borglum, A.D., Mors, O., Breen, G., Lee, P.H., Kendler, K.S., Smoller, J.W., Tucker-Drob, E.M., Nivard, M.G., 2020. Genetic architecture of 11 major psychiatric disorders at biobehavioral, functional genomic, and molecular genetic levels of analysis. *medRxiv*. 2020.2009.2022.20196089.
- Hall, W., 2017. Socioeconomic status and susceptibility to alcohol-related harm. *Lancet Public Health* 2, e250–e251.
- Hasin, D.S., Grant, B.F., 2015. The national epidemiologic survey on alcohol and related conditions (NESARC) waves 1 and 2: review and summary of findings. *Soc. Psychiatry Psychiatr. Epidemiol.* 50, 1609–1640.
- Hasin, D.S., Liu, X., Nunes, E., McCloud, S., Samet, S., Endicott, J., 2002. Effects of major depression on remission and relapse of substance dependence. *Arch. Gen. Psychiatry* 59, 375–380.
- Haugland, S.H., Holmen, T.L., Krokstad, S., Sund, E.R., Bratberg, G.H., 2015. Intergenerational hazardous alcohol use and area factors: the hunt study, Norway. *Subst. Use Misuse* 50, 1753–1764.
- Hummer, R.A., Lariscy, J.T., 2011. Educational Attainment and Adult mortality. *International handbook of Adult Mortality*. Springer, pp. 241–261.
- Kendler, K.S., Prescott, C.A., Myers, J., Neale, M.C., 2003. The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Arch. Gen. Psychiatry* 60, 929–937.
- Keyes, K.M., Krueger, R.F., Grant, B.F., Hasin, D.S., 2011. Alcohol craving and the dimensionality of alcohol disorders. *Psychol. Med.* 41, 629–640.
- Knol, M.J., VanderWeele, T.J., 2012. Recommendations for presenting analyses of effect modification and interaction. *Int. J. Epidemiol.* 41, 514–520.
- Kohler, C.A., Evangelou, E., Stubbs, B., Solmi, M., Veronese, N., Belbasis, L., Bortolato, B., Melo, M.C.A., Coelho, C.A., Fernandes, B.S., Olfson, M., Ioannidis, J.P.A., Carvalho, A.F., 2018. Mapping risk factors for depression across the lifespan: an umbrella review of evidence from meta-analyses and Mendelian randomization studies. *J. Psychiatr.* 163, 189–207.
- Koob, G.F., Volkow, N.D., 2016. Neurobiology of addiction: a neurocircuitry analysis. *Lancet Psychiatry* 3, 760–773.
- Li, J., Wang, H., Li, M., Shen, Q., Li, X., Zhang, Y., Peng, J., Rong, X., Peng, Y., 2020. Effect of alcohol use disorders and alcohol intake on the risk of subsequent depressive symptoms: a systematic review and meta-analysis of cohort studies. *Addiction* 115, 1224–1243.
- Lund, C., Brooke-Sumner, C., Baingana, F., Baron, E.C., Breuer, E., Chandra, P., Haushofer, J., Herrman, H., Jordans, M., Kieling, C., Medina-Mora, M.E., Morgan, E., Omigbodun, O., Tol, W., Patel, V., Saxena, S., 2018. Social determinants of mental disorders and the Sustainable development goals: a systematic review of reviews. *Lancet Psychiatry* 5, 357–369.
- Martinez, P., Neupane, S.P., Perlestenbakken, B., Toutoungi, C., Bramness, J.G., 2015. The association between alcohol use and depressive symptoms across socioeconomic status among 40- and 45-year-old Norwegian adults. *BMC Public Health* 15, 1146.
- McHugh, R.K., Weiss, R.D., 2019. Alcohol use disorder and depressive disorders. *Alcohol Res.* 40.
- Melchior, M., Chastang, J.F., Head, J., Goldberg, M., Zins, M., Nabi, H., Younès, N., 2013. Socioeconomic position predicts long-term depression trajectory: a 13-year follow-up of the GAZEL cohort study. *Mol. Psychiatry* 18, 112–121.
- National Institutes of Mental Health, 2017. Past year prevalence of major depressive episode among U.S. adults aged 18 or older in 2017. <https://www.nimh.nih.gov/health/statistics/major-depression.shtml> (accessed 12/03/2021).
- Paris, J., 2014. The mistreatment of major depressive disorder. *Can. J. Psychiatry* 59, 148–151.
- Peen, J., Schoevers, R.A., Beekman, A.T., Dekker, J., 2010. The current status of urban-rural differences in psychiatric disorders. *Acta Psychiatr. Scand.* 121, 84–93.
- Probst, C., Kilian, C., Sanchez, S., Lange, S., Rehm, J., 2020. The role of alcohol use and drinking patterns in socioeconomic inequalities in mortality: a systematic review. *Lancet Public Health* 5, e324–e332.
- Probst, C., Roerecke, M., Behrendt, S., Rehm, J., 2014. Socioeconomic differences in alcohol-attributable mortality compared with all-cause mortality: a systematic review and meta-analysis. *Int. J. Epidemiol.* 43, 1314–1327.
- Rehm, J., Gmel Sr, G.E., Gmel, G., Hasan, O.S.M., Imtiaz, S., Popova, S., Probst, C., Roerecke, M., Room, R., Samokhvalov, A.V., Shield, K.D., Shuper, P.A., 2017. The relationship between different dimensions of alcohol use and the burden of disease—an update. *Addiction* 112, 968–1001.
- Research Triangle Institute, 2018. Software for Survey Data Analysis (SUDAAN) SAS-Callable Version 11.0.3. Research Triangle Institute. Research Triangle Park, NC.
- Saha, T.D., Chou, S.P., Grant, B.F., 2006. Toward an alcohol use disorder continuum using item response theory: results from the national epidemiologic survey on alcohol and related conditions. *Psychol. Med.* 36, 931–941.
- SAMHSA Center for Behavioral Health Statistics and Quality, 2019. 2019 national survey on drug use and health. Table 5.4B <https://www.samhsa.gov/data/sites/default/files/reports/rpt29394/NSDUHDetailedTabs2019/NSDUHDetailedTabsSect5pe2019.htm#tab5-4a> (accessed 07/03/2021).
- Sarvet, A., Wall, M., 2016. Additive interaction in SUDAAN. http://www.columbia.edu/~mmw2177/Additive%20interaction%20in%20SUDAAN_08032016.pdf (accessed 09/07/2021).
- Sasson, I., Hayward, M.D., 2019. Association between educational attainment and causes of death among white and black US adults, 2010–2017. *JAMA* 322, 756–763.
- Shanahan, L., Copeland, W.E., 2021. Psychiatry and deaths of despair. *JAMA Psychiatry*.
- Shanahan, L., Hill, S.N., Gaydos, L.M., Steinhoff, A., Costello, E.J., Dodge, K.A., Harris, K.M., Copeland, W.E., 2019. Does despair really kill? A roadmap for an evidence-based answer. *Am. J. Public Health* 109, 854–858.
- Shiels, M.S., Tatalovich, Z., Chen, Y., Haozous, E.A., Hartge, P., Nápoles, A.M., Pérez-Stable, E.J., Rodriguez, E.J., Spillane, S., Thomas, D.A., Withrow, D.R., Berrington de González, A., Freedman, N.D., 2020. Trends in mortality from drug poisonings, suicide, and alcohol-induced deaths in the United States from 2000 to 2017. *JAMA Netw. Open* 3, e2016217–e2016217.
- StataCorp, 2021. Stata Statistical Software: Release 17. StataCorp LLC, College Station, TX.
- Substance Abuse and Mental Health Services Administration, 2019. Key substance use and mental health indicators in the United States: results from the 2018 national survey on drug use and health. <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHNationalFindingsReport2018/NSDUHNationalFindingsReport2018.pdf> (accessed 07/03/2021).
- Turner, S., Mota, N., Bolton, J., Sareen, J., 2018. Self-medication with alcohol or drugs for mood and anxiety disorders: a narrative review of the epidemiological literature. *Depress. Anxiety* 35, 851–860.
- Walsemann, K.M., Gee, G.C., Ro, A., 2013. Educational attainment in the context of social inequality: new directions for research on education and health. *Am. Behav. Sci.* 57, 1082–1104.