**ORIGINAL RESEARCH** 



## The Role of Despair in Predicting Self-Destructive Behaviors

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#### 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

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#### Introduction

Following nearly a century of almost uniform improvements in life expectancy, in 2015 the US began to reverse course, with overall annual declines for 2015, 2016, and 2017 (Kochanek et al., 2017; Murphy et al., 2016; Xu et al., 2016). Increases in working age (ages 25–64) mortality contributed to this reversal (Case & Deaton, 2015; Harris et al., 2021; National Academies of Sciences Engineering & Medicine, 2021), including deaths due to drug overdose linked to the opioid epidemic (Glei & Preston, 2020; Masters et al., 2017a). Death by suicide and alcohol-related liver disease increased as well (National Academies of Sciences et al., 2021), and declines in cardiovascular disease mortality stalled (Mehta et al., 2020). Although this population trend was initially concentrated among non-Hispanic White Americans with low educational attainment (Case & Deaton, 2015), it has since been observed across race/ethnicity (Friedman et al., 2023; Harris et al., 2021; National Academies of Sciences Engineering & Medicine, 2021; Woolf & Schoomaker, 2019; Woolf et al., 2018; Zang et al., 2019).

There are many explanations for this pattern of increasing mortality in midlife due to suicide, drug abuse, and alcohol use, ranging from declines in collective efficacy, deindustrialization and the erosion of the American working class, changes in family formation, supply-side factors in the opioid crisis, and an underlying feeling of hopelessness and despair among non-Hispanic White Americans with low educational attainment (Case & Deaton, 2020; Cherlin, 2018; Glei & Weinstein, 2019; Glei et al., 2018, 2019, 2020; Goldman et al., 2018; Siddiqi et al., 2019; Venkataramani et al., 2019; Wuthnow, 2018). Regardless of the exact structural and institutional factors, these secular trends are internalized by individuals and operate through despair and subsequent self-destructive coping behaviors. In fact, the cluster of causes of death due to suicide, drug overdose, and alcohol-related liver disease is referred to as the "deaths of despair" (Case & Deaton, 2017) because the behaviors that lead to these causes of death are self-destructive and postulated to reflect hopelessness.

Despite the central role of despair in common explanations for rising midlife mortality, this explanation has largely gone unexamined empirically, perhaps on account of its conceptual complexity (for exception see Copeland et al., 2020; Gutin et al., 2023). Such empirical tests are particularly important as some studies suggest rising levels of depression and anxiety in recent cohorts (Gaydosh et al., 2019; Glei et al., 2020; Goldman et al., 2018); if despair is indeed responsible for increasing mortality, we might expect new cohorts entering midlife to experience even greater survival challenges. Moreover, a test of the role of despair in the etiology of substance use behaviors and mental health outcomes can help us better understand the current crisis in midlife health and design more effective policies and interventions to improve population health outcomes (Brennan et al., 2023; Godwin, 2020; Na et al., 2022). Drawing on appropriate theory, measures, and methods, we empirically assess the role of despair in predicting the self-destructive behaviors that precede causes of death due to suicide, drug abuse, and alcohol-related liver disease.

In this study, we use a data-driven supervised machine learning approach. Supervised machine learning uses a subset of data with inputs or predictors (called features) and outcomes, and iteratively learns the best way to predict the outcome using

the features. After training on a subset of data, the best prediction model is then applied to a holdout or test set of data to determine how the model performs on data that it has never "seen". Machine learning methods relax the assumptions required for inference in classical statistical models in favor of predictive performance and are able to accommodate greater complexity, such as multidimensional interactions among variables (Breiman, 2001). This is a particularly useful method for examining multi-dimensional constructs like despair, where we can draw on theory to identify plausible inputs but require more complex modeling strategies to identify how they are interrelated and the extent to which these inputs vary in their relative importance/ contributions. There is empirical support for this approach as well; traditional statistical approaches often fail to accurately predict suicidal thoughts and behaviors, particularly in the short term, with models based on expert knowledge doing no better than chance (Huang et al., 2017). Recent applications of machine learning approaches to predicting suicidal ideation demonstrate improved performance compared to clinical prediction (Fox et al., 2019; Linthicum et al., 2019; Ribeiro et al., 2019; Walsh et al., 2017, 2018). Several studies apply machine learning to predict substance use, demonstrating the relevance of psychological and health status across the life course (Hu et al., 2020; Jing et al., 2020).

We define despair as hopelessness that manifests across four domains: emotional, cognitive, biosomatic, and behavioral (Shanahan et al., 2019). We use random forest and LASSO regression to predict four different self-destructive behavioral outcomes—suicidal ideation, heavy drinking, illegal drug use, and prescription drug abuse—measured at the start of midlife (ages 33–43) using Wave V data from the nationally representative National Longitudinal Study of Adolescent to Adult Health (Add Health). Our analysis tests the relevance of despair across different behaviors, as is proposed by the hypothesis that feelings of despair are leading to a cluster of different causes of death. 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? In answering both questions, we examine differences across the four outcomes. Differences in prediction accuracy, feature importance, and relevant domains would suggest a differential role of despair in driving these behaviors, whereas consistent prediction and importance of domains would provide support for the hypothesis of a common underlying cause.

#### Background

The recent declines in life expectancy in the United States are driven by more sustained increases in mortality, particularly among working age (25–64) individuals, that began around the turn of the twenty-first century for those in midlife and expanded to those in young and established adulthood in the last decade (Ho, 2013; Ho & Preston, 2010; Montez & Zajacova, 2013; National Academies of Sciences Engineering & Medicine, 2021; Woolf & Schoomaker, 2019). Documenting part of this rise in midlife mortality, Case and Deaton observed notable increases in deaths due to drug overdose, alcohol-related liver disease, and suicide, and later described this cluster of causes "deaths of despair" (Case & Deaton, 2015, 2017, 2020). Despair, or a sense of hopelessness, may be caused by labor market changes that increase economic insecurity and social isolation, stagnant wages, and lower intergenerational mobility, both real and perceived. In response to their pain and distress, individuals turn to self-destructive coping behaviors like excessive alcohol use, prescription drug abuse and illegal drug use, and self-harm (Case & Deaton, 2020). The availability of prescription opioids during this period served as a backdrop for what has been described as a demand hypothesis driven by changes in the labor market wrought by globalization and deindustrialization on a particular cohort of Americans (King et al., 2022; Verdery et al., 2020). As Case and Deaton explain, "grouping deaths from suicide, alcohol, and drugs captures a common underlying cause—despair—that is not easily captured when they are treated separately" (2020, p. 96).

Yet despair as an explanatory framework for rising mortality presents several complications and challenges, as others have noted (Diez Roux, 2017; Harper et al., 2021; Shanahan et al., 2019). Our primary concern is the lack of conceptual clarity and empirical evidence regarding the definition, measurement, and effect of despair (Harper et al., 2021; Shanahan et al., 2019). Case and Deaton explain their use of the term: "We call the three kinds of death 'deaths of despair.' It is a convenient label, indicating the link with unhappiness, the link with mental or behavioral health, and the lack of any infectious agent, but it is not intended to identify the specific causes of despair" (2020, p. 40). While the underlying cause of despair is indeed unspecified, the hypothesized role of despair in driving these causes of death is explicit. Regardless of why individuals are feeling hopeless, the despair hypothesis suggests that they turn to substance use and harmful behaviors in response to those feelings; "Suicides are deaths of despair. But the circumstances that can lead to suicide find less extreme forms when people turn to drugs or alcohol to seek refuge from pain, loneliness, and anxiety. Drugs and alcohol can induce a euphoria that, at least temporarily, may relieve physical and mental pain" (Case & Deaton, 2020, p. 95). With an unknown cause and in the absence of a clear conceptualization, despair may only be inferred based on self-destructive health behaviors and specific causes of death; as Gutin et al. describe, "extant research continues to promote a tautological conceptualization of despair as being inferred from its outcomes rather than being examined as a standalone construct" (2023, p. 2). Harper et al. express concern that despair is "a vague term, rarely defined and even less frequently measured" (2021, p. 383). In our previous work, we argue that the lack of a clear definition of despair stymies research in this area and precludes serious tests of the despair hypothesis (Shanahan et al., 2019).

This lack of conceptual clarity—and how this translates into measurement and subsequent empirical analysis—may lead to "mixed" findings that draw the role of despair further into question. Three additional limitations in the explanatory power of despair arise from further interrogation of the empirical patterns of midlife mortality. First, there is considerable heterogeneity in the sociodemographic patterns of mortality by these causes by age, race/ethnicity, education, and geography that are difficult to explain by one common cause (Harper et al., 2021; Monnat, 2023; Monnat & Brown, 2017; Rigg et al., 2018; Sasson, 2016; Sasson & Hayward, 2019; Woolf et al., 2018). From subsequent work it is clear that the mortality patterns are not restricted to non-Hispanic White adults with low educational attainment, as originally described, but mortality increases are now even larger among minoritized racial/eth-

nic groups (Alexander et al., 2018; Woolf & Schoomaker, 2019). Reliance on the despair framework threatens to obscure or minimize large and enduring disparities by race/ethnicity. Second, there is evidence that increases in overall midlife mortality and lagging US life expectancy are driven by drug-related deaths, highlighting this cause as distinct from suicide and alcohol-related deaths (Ho, 2019; Masters et al., 2017a, 2017b; Simon & Masters, 2021). Rather than a cohort experience, the age pattern and timing of overdose mortality likely reflects a period exposure, specifically the opioid epidemic (Tilstra et al., 2021). Such findings cast doubt on whether the three causes of death can be explained by a shared origin. Third, while acknowledging the role of stagnating cardiovascular disease mortality in allowing drug, alcohol, and suicide mortality to reverse progress in midlife mortality, despair does not offer an explanation for observed patterns in cardiovascular disease (Mehta et al., 2020).

Notably, despair is not a well-defined psychological concept for which there is an established construct to measure. In this paper, we draw from one conceptualization of despair as manifesting across four domains-emotional, cognitive, behavioral, and biosomatic (Shanahan et al., 2019). The distinction between domains is conceptual and intended to guide our selection of features as well as to consider the pathways through which despair may influence distinct self-destructive behaviors. Emotional despair encompasses feelings and sentiments, including sadness, loneliness, and anhedonia, such as depressive symptoms. Cognitive despair refers to thoughts indicating pessimism, hopelessness, and worthlessness, such as lack of hope for the future and a lack of self-confidence. Behavioral despair captures acts that demonstrate a lack of consideration for the future, such risky sexual behavior, reckless driving, or criminal activity. Note that we do not include prior measures of the outcome behavior in our operationalization of behavioral despair (i.e. heavy drinking in adolescence predicting heavy drinking in adulthood); we instead categorize prior behaviors of the outcomes as their own predictor set. Biosomatic despair reflects the physiological consequences of repeated and chronic activation of the stress response system, such as allostatic load or physiological wear and tear. Working from this conceptualization, it is possible to make progress in the measurement of despair. It is not our goal in this manuscript to evaluate the measurement of despair; rather, we work from this conceptualization to derive a broad measure of despair that provides a generous test of the despair hypothesis that moves beyond previous operationalizations that include single proxy measures for despair such as labor force attachment or psychological distress (Glei et al., 2024; Zheng et al., 2023). Gutin et al. use a structural equation modeling approach to demonstrate that it is possible to measure despair and its constituent domains derived from this conceptual framework (Gutin et al., 2023). Results from their models provide empirical support for all four domains as distinct latent concepts-or "dimensions" of despair. However, these latent dimensions of despair are also highly *correlated* with one another (particularly the emotional and cognitive), such that a model where all four dimensions are instead indicators of a higher-order latent construct of "overall" despair exhibits excellent fit, thus empirically supporting a conceptualization of despair as a multi-dimensional latent construct.

Beyond definition and measurement, it remains unclear whether despair is related to the behaviors that precede death due to suicide, drug overdose, and alcohol-related causes. There are few empirical tests in the literature; the two extant studies both find important differences in the relationship between despair and self-destructive behaviors. To our knowledge, there is only one empirical demonstration that despair predicts mortality from the "deaths of despair" (Gutin & Gaydosh, 2025). With respect to behavioral outcomes, Copeland et al. find higher cognitive despair is associated with suicidal ideation and behavior and illegal drug and opioid use, but not alcohol problems (2020). Similarly, Gutin et al. find the strongest association between despair and suicidal ideation, and the weakest association between despair and heavy drinking (2023).

Though conceptual and empirical clarity are needed, considering the social and economic changes observed in the United States in recent decades and parallel decline in key population health measures, the theoretical case for despair continues to be compelling. Continued work is necessary to refine our understanding of despair and understand its limitations. We contribute to this growing body of work a data-driven empirical assessment of the relationship between despair and self-destructive behaviors. In evaluating the role of despair, we compare the performance of machine learning models predicting four self-destructive behaviors and the importance of different measures and domains of despair. To address our first research question-whether despair predicts the behaviors that are antecedent to death by suicide, alcohol-related liver disease, and drug overdose—we take two approaches that both rely on comparison of model performance. First, within a given behavioral outcome, we evaluate model performance using all available measures of despair prior to the measurement of the outcome. We compare this performance to models using two other sets of predictors: (1) clinical risk factors measured concurrently with the outcomes, and (2) measures of the behavior prior to the measurement of the outcome (Appendix Tables 2 and 3). We consider predictor sets 1 and 2 as benchmark models and evaluate whether despair outperforms or improves our prediction of each outcome. This approach allows us to evaluate whether despair predicts a given behavioral outcome, and how good that prediction is relative to established risk factors. Second, across the four behavioral outcomes, we compare model performance using the same set of despair predictors. We expect similar predictive performance across outcomes if despair is similarly associated.

For our second research question—which features and domains of despair are most important—we also take two approaches, now relying on comparison of feature importance. First, we compare the ranked feature importance across the four outcomes from models with the same set of despair predictors. If despair were similarly related to the behaviors, we expect consistency in the ranked importance of the features. Second, we consider not just the individual features, but the domains of despair that they reflect, and compare the average feature importance for each domain across outcomes. Again, we expect that consistency in the importance of the domains across outcomes supports a similar process whereby despair influences selfdestructive behavior.

Defining and operationalizing a multidimensional measure of despair allows for an empirical test of the potential role of despair in the behaviors that contribute to elevated midlife mortality. This work extends our understanding of the etiology of midlife mortality by moving beyond single individual measures of psychosocial dis-

Table 1         Sample descriptive	Male	41%
statistics	White	62%
	Black	18%
	Hispanic	13%
	Asian	6%
	Other	1%
	Caregiver education	
	High school or less	43%
	Some college	30%
	College or more	27%
	Individual education	
	High school or less	18%
	Some college	42%
	College or more	40%
	Wave V behavioral outcomes	
	Suicidal ideation	6%
	Heavy drinking	13%
	Illegal drug use	3%
	Prescription drug abuse	11%
	n=	6158

tress and considering multiple behavioral outcomes. Findings from this study may help inform interventions designed to reduce self-destructive behaviors by demonstrating shared and distinct life course predictors.

#### **Data and Methods**

We use data from the National Longitudinal Study of Adolescent to Adult Health (Add Health), an ongoing longitudinal study representative of US adolescents in grades 7–12 in 1994/1995, with follow up at Wave III (2001–2002), Wave IV (2008–2009), and Wave V (2016–2018) (35). We use data from individuals who participated in Waves I, III, IV, and V with complete information on all included variables (n=6158) (Table 1). As we present in Appendix Table 2, our analytic sample has a slightly lower proportion of male respondents, and more White respondents (fewer Black and Hispanic respondents), compared to the overall Wave V Add Health sample.

#### Outcomes

We predict four dichotomous measures reflecting the behaviors proximal to death by suicide, drug overdose, and alcohol-related disease. These measures were based on self-report at Wave V, when respondents were 33–43 years old (Table 1). Suicidal ideation is an indicator of whether the respondent seriously thought about committing suicide in the past 12 months; 6% of respondents report suicidal ideation.<sup>1</sup> Heavy drinking is an indicator of whether the respondent reports drinking 15 or more (men)

 $<sup>^{1}</sup>$ Add Health asks about suicide attempts in the last year; this is a very rare event, with  $\sim 1\%$  of respondents reporting suicide attempt. We therefore do not include suicide attempt as an outcome in this analysis.

or 8 or more (women) drinks per week in the last month; 13% of respondents report heavy drinking. Illegal drug use is an indicator of any illegal drug use, including cocaine, crystal meth, heroin, or any other type, in the last 30 days; 3% of respondents report illegal drug use. Prescription drug abuse is an indicator of any prescription drug abuse/misuse (taking more than prescribed or medicine not prescribed), including sedatives, tranquilizers, stimulants, and painkillers, in the last 30 days; 11% of respondents report prescription drug abuse.

#### Predictors

Our primary interest is in testing the role of despair. We use all available measures related to despair at Waves I, III, and IV (preceding the measurement of our outcomes at Wave V). This manual variable selection was based on our reading of the prior literature, domain expertise, and established psychometric scales. We divide these predictors into the four domains of despair: emotional, cognitive, biosomatic, and behavioral (Appendix Table 4). Diagnosed depression and anxiety, as well as items from the CES-D depressive symptom scale and measures of anxiety symptoms are included as emotional despair. Measures of optimism, hopelessness, withdrawal, and sense of control over life are included as cognitive despair. Obesity, self-rated health, and physical limitations are included as biosomatic despair. School delinquency, physical violence, criminal behavior, incarceration, and social integration are included as behavioral despair. Nearly all predictors are binary or categorical, as random forests can be sensitive to continuous measures with high variation. There are 219 despair predictors in total. In testing the importance of despair and its domains, we exploit the flexibility of the machine learning approaches and do not create an aggregate or summary measure of despair, but rather include each predictor individually. The frequency of each despair predictor varies widely from less than 1% of the sample reporting things like violent crime engagement to more than 60% reporting labor market participation.

As mentioned in our approach, we evaluate despair against two other sets of predictors: (1) clinical risk factors and (2) measures of the outcome behavior at prior waves. The clinical predictors are selected from the literature on screening tools used to evaluate risk for suicide (Gaynes et al., 2004), alcohol abuse (Ewing, 1984), and drug abuse (Skinner, 1982; Yudko et al., 2007) (Appendix Table 2). We measure these variables at Wave V, as clinical screening would inquire about recent events and experiences. We use measures of each outcome behavior at prior waves, referring in figures to these variables by the shorthand diseases of despair, or DOD (I, III, and IV; Appendix Table 3). For suicidal ideation and heavy drinking, the measures are the same at all waves. For illegal drug use, we also include a measure of whether the respondent ever used any illegal drugs at Wave I, in addition to the measures that reflect use in the last 30 days. Prescription drug use was not asked at Wave I, and we therefore only include measures at Waves III and IV.

We present the correlation among all the variables in Fig. 1 (and by domain in Appendix Figs. 8, 9, 10, and 11). There are expected patterns with high correlation among variables in the same domain and measured in the same wave. Across domains, emotional and cognitive despair are most closely correlated, and Wave IV



Fig. 1 Correlation between predictor and outcome variables, with domains (black) and waves (grey) of measurement indicated in squares

measures of behavioral despair correlated more strongly with prior self-destructive behaviors.

### **Other Controls**

We include basic demographic characteristics of biological sex measured as male or female; self-reported race/ethnicity measured as non-Hispanic White, non-Hispanic Black, Hispanic, Asian, and other; and socioeconomic status as measured by parental educational attainment at Wave I and individual educational attainment at Wave IV categorized as high school or less, some college, or college degree or more (Table 1). We use educational attainment rather than income because it is a more stable indicator of socioeconomic status across childhood and adulthood, and has less missing data than income.

#### Methods

We apply two supervised machine learning methods—random forest and LASSO regression—to predict the four dichotomous outcomes. The two approaches have complementary strengths. Random forest models are good at prediction and accom-

modate nonlinearities in relationships, which makes the approach particularly appropriate for our first research question, which focuses on prediction. LASSO regression is useful for feature selection and interpretation of relationships between features and outcomes, which makes the approach well-suited for our second research question. We use the two methods to address both research questions in order to most flexibly model the outcomes as well as determine that our results are not sensitive to the particular classification algorithm used for prediction.

The first method we apply is random forests. A common technique for classification (prediction of a dichotomous outcome) is the decision tree. Using decision trees, a sample is recursively partitioned with the goal of creating the most homogenous group by outcome, resulting in an inverted tree that has roots, branches, and leaves. Here, each root represents a test, each branch represents a split in the data by some attribute or feature, and each leaf denotes the predicted outcome. Decision trees are useful because they can be used with large and complex datasets without imposing a complicated parametric structure. Every observation is assigned a predicted outcome by following the path from the top-most root node down to internal branch nodes and eventually to the terminal leaf nodes. A random forest is a collection of decision trees where the classification algorithm draws multiple bootstrap samples from the training dataset and fits a decision tree on each. Each tree in the random forest generates a prediction for each observation, and the proportion of votes of for each class are used to generate a score. Following the production of this score, a threshold is applied to determine the predicted class of the observation. We implement random forest in R using the ranger package (https://github.com/imbs-hl/ranger).

The second method we apply is LASSO logistic regression. LASSO stands for least absolute shrinkage and selection operator and is a form of regularized or penalized regression where regularization is used to solve overfitting of the model to the training data. In LASSO regression, we add a penalty term equal to the absolute value of the sum of the coefficients. The constraint effectively shrinks coefficients to zero for features that are not contributing sufficiently to the overall fit of the model relative to the penalization; this characteristic of LASSO regression addresses our goal of understanding the most important aspects and domains of despair for predicting the outcome behaviors. The strength of this constraint is controlled by a tuning parameter denoted by  $\lambda$  (lambda); a larger  $\lambda$  will result in more coefficient shrinkage. We implement this estimation using the glmnet package in R (https://glmnet.stanford.edu/).

For both approaches, our methodology proceeded in the following manner. We first split the data into training and test subsamples (75/25 percent split), stratified to provide a similar distribution of the outcome in both subsamples. In the training set, we used tenfold cross validation to tune the hyperparameters, selecting those that provide the best prediction measured using the area under (AUC) the receiver operating characteristic (ROC) curve. We then estimate the final model parameters and use the final model to predict the outcomes in the test set. We evaluate the performance of the final model in the test data that had not been used in training the model using the AUC. ROC curves plot the true positive rate against the false positive rate; AUC reflects the overall performance of the model and the ability to discriminate between positive and negative cases, with 0.5 no better than chance, and 1 perfect prediction.

To calculate the feature importance of our predictors in the random forest model, we use the mean decrease in impurity (MDI). Impurity is a Gini measure that is used to determine tree branching and captures how often a case would be incorrectly classified if it were randomly assigned based on the distribution of the outcome in the subset of data at the node where the split occurs. The decrease in impurity that occurs as a result of the split is averaged across all trees in the random forest where, and proportional to the sample size that reaches each node. Feature importance for the LASSO models is determined by the absolute value of the standardized coefficient from the model.

#### Results

#### Predicting Self-Destructive Behaviors: Model Performance

We first investigate whether despair predicts the self-destructive behaviors that precede death by suicide, alcohol-related liver disease, and drug overdose. Within each behavioral outcome, we compare model performance by predictor set, with despair predictors in model 1, clinical predictors in model 2, and measures of the behaviors at prior waves in model 3. We test for statistical significance in the difference between the AUC achieved for each model in comparison to model 1 (p < 0.05). We present the results in Fig. 2 (random forest) and Fig. 3 (LASSO).

The best prediction of suicidal ideation is achieved with the clinical predictors for both the random forest and the LASSO model (AUC 0.75 and 0.80). The difference



**Fig. 2** Receiver operating characteristic (ROC) curves with area under the curve (AUC) indicated in the legend for results from random forest models 1–3 predicting suicidal ideation, heaving drinking, illegal drug use, and prescription drug abuse. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001 for tests of statistical significance comparing AUC for each model to model 1



**Fig. 3** Receiver operating characteristic (ROC) curves with area under the curve (AUC) indicated in the legend for results from LASSO models 1–4 predicting suicidal ideation, heaving drinking, illegal drug use, and prescription drug abuse. \*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001 for tests of statistical significance comparing AUC for each model to model 1

between the clinical predictor set model performance and the despair model performance is not statistically significant for either the random forest or LASSO model.

The clinical predictor set provides the best prediction of heavy drinking in the random forest model (AUC 0.77), and it is significantly different from prediction using the despair set alone. The prior self-destructive behaviors (DOD) predictor set provides the best prediction of heavy drinking in the LASSO model (AUC 0.78), and it is significantly different from prediction using the despair set alone. Model 1, using just the despair predictor set, offers the worst prediction of heavy drinking using both the random forest (0.64) and the LASSO (0.69).

The despair predictor set provides the best prediction of illegal drug use with the random forest model (AUC 0.77), while the prior self-destructive predictor set provides the best prediction with the LASSO model (AUC 0.76). However, the differences between the clinical and prior self-destructive behaviors predictor sets compared to the despair predictor set in model 1 are not statistically significant with either the random forest or the LASSO estimation.

The prior self-destructive behaviors predictor set provides the best prediction of prescription drug abuse using both the random forest and LASSO model (AUC 0.69 and 0.68). However, the performance is not significantly different from the despair predictor set in model 1 using either estimation approach.

Comparing model performance across the four behavioral outcomes using the same despair set of predictors (model 1) (Fig. 4), we find variation in the random forest models (AUC 0.72 suicidal ideation, 0.64 heavy drinking, 0.77 illegal drug use, 0.67 prescription drug abuse). There is similar though less variation in classification of the outcomes from the LASSO models (AUC 0.77 suicidal ideation, 0.69 heavy



**Fig. 4** Receiver operating characteristic (ROC) curves with area under the curve (AUC) indicated in the legend for results from random forest and LASSO models predicting heaving drinking, illegal drug use, prescription drug abuse, and suicidal ideation using the despair predictors (corresponding to model 1 in Figs. 2 and 3)

drinking, 0.75 illegal drug use, 0.67 prescription drug abuse). Despair predicts the four behavioral outcomes differently using the same set of predictors with both the random forest and the LASSO classification approaches.

# The Importance of Despair in Predicting Self-Destructive Behaviors: Feature Importance

Turning to our second research question, what measures and domains of despair are most important in predicting the behavioral outcomes? In answering this question, we examine the ranked feature importance for the model with despair predictors using both the random forest and LASSO. In Fig. 5, we plot the top ten most important features for each outcome. In terms of the specific measures, there is modest overlap between the top ten features in the random forest and the LASSO for each outcome. Depression diagnosis ranks in the top ten features for predicting suicidal ideation with both the random forest and LASSO. Tobacco use, religious service attendance, and arrest history rank in the top ten features for predicting heavy drinking with both the random forest and LASSO. Marijuana use ranks in the top ten features for predicting illegal drug use in both the random forest and LASSO. There is no overlap in the top ten features for predicting prescription drug use.

The overlap between random forest and LASSO top ten feature importance is more pronounced when considering the domains of the predictors. For suicidal ideation, the predictors are from a mix of emotional, cognitive, and behavioral domains. The top ten important features for heavy drinking are predominantly from the behavioral despair domain, with a few cognitive despair features. Behavioral despair features predominate the top ten important features for illegal drug use, with some emotional despair features in the LASSO model. The results between the random forest and LASSO are less consistent for prescription drug misuse, which include a mix of behavioral, biosomatic, and emotional despair in the random forest, and emotional, behavioral, and cognitive despair in the LASSO.



**Fig. 5** Top ten important features by domain for each outcome from random forest and LASSO models (model 1). Lines map features that are shared in the top ten across the random forest and LASSO. Features in *bold/italic* appear in the top ten across multiple outcomes

We investigate broader patterns by the corresponding domains of despair of each feature across the entire predictor set for all outcomes (Figs. 6 and 7; detailed in Appendix Figs. 12, 13, 14, 15, 16, and 17). The first thing to note is the large spread in importance across outcomes. With the random forest, cognitive despair features have mixed importance across all four outcomes. Emotional despair features are often ranked highly important for suicidal ideation, followed by prescription drug abuse, but less so for heavy drinking and illegal drug use. Biosomatic despair features. Behavioral despair features are ranked highly for prescription drug misuse but vary widely for other outcomes. Behavioral despair features are ranked highly for the outcomes. With the LASSO, there is even more spread in the ranked importance, and the patterning within domain by outcome is less apparent.

This is confirmed when considering the average ranked importance by domain (Appendix Table 5). With the random forest, emotional and cognitive despair have higher average importance for suicidal ideation. Cognitive despair features have higher average importance for heavy drinking, illegal drug use, and prescription drug abuse. In contrast, with the LASSO the average ranked importance is more similar across cognitive, emotional, behavioral, and biosomatic despair domains for all outcomes; this likely reflects the LASSO shrinkage strategy for related variables, resulting in more similar average importance across domains.

#### **Discussion and Conclusion**

Does despair predict the self-destructive behaviors that precede death by suicide, alcohol-related liver disease, and drug overdose? In short, it depends on the behavior; our ability to predict the four self-destructive behaviors varies widely. Within outcome, measures of despair are better able to predict prescription drug abuse and illegal drug use, while suicidal ideation and heavy drinking are more accurately



Fig. 6 Importance rank based on mean decrease in impurity by domain for each outcome from random forest models including despair predictors

predicted by clinical risk factors and prior self-destructive behaviors, respectively. While precise performance results vary depending on the algorithm employed, our results are consistent in terms of relative performance, lending greater confidence to our findings. Using thresholds common with medical diagnostic tests, despair's prediction of illegal drug use can be considered excellent (AUC>0.80), while despair's prediction of heavy drinking is poor (AUC<0.70) (Mandrekar, 2010). If despair were similarly driving each behavior, we would expect similar prediction across the outcomes. Instead, despair is implicated much more strongly for drug use behaviors— both illegal and prescription—compared to suicidal ideation and heavy drinking. This pattern is consistent with demographic research emphasizing distinct patterns



Fig. 7 Importance rank based on absolute value of the standardized coefficient by domain for each outcome from LASSO models including despair predictors

in drug-related mortality compared to alcohol and suicide mortality (Masters et al., 2017b). Individuals experiencing despair may turn to drug use for self-medication and temporary relief, and our measures of drug use may better capture this purpose than the measure of heavy drinking, which likely captures both normative social and disordered use (Azagba et al., 2020; Merrill et al., 2023; Turner et al., 2018). Differences in the predictive power of despair across behavioral outcomes is important because it suggests that the determinants of such behaviors are likely distinct, and as such would require distinct interventions to address.

What measures and domains of despair are most important in predicting the behavioral outcomes? The importance of different measures of despair and the contribution of different domains of despair varies depending on the outcome predicted. Emotional despair ranks more highly for suicidal ideation, while behavioral despair ranks more highly for illegal drug use, particularly with the random forest model. The most consistent pattern is the very wide variety in feature importance across outcomes. This finding suggests that the pathways from despair to self-destructive behaviors, and potentially ultimately to mortality, are distinct, and despair in particular domains may be more likely to manifest in certain behaviors that are more closely aligned with a given domain. Specifically, feelings of loneliness, sadness, and depression are more strongly implicated in the pathway to suicide, whereas externalizing and risky behaviors are implicated in illegal drug use and potential overdose. Such patterns may inform potential interventions targeted at suicide prevention or drug use by directing attention to emotional versus behavioral risk factors and pathways.

Critically, while there is perhaps less utility in thinking about despair as a "homogenous" risk factor-particularly underlying multiple recent demographic trendsthere is a strong case to be made that recognizing the multi-dimensionality of despair, and its manifestation in different forms, provides a much-needed and valuable source of nuance to its conceptualization with utility for both demographic research and population health practice. That is, much of the scientific discourse on despair has focused on a binary evaluation of the "deaths of despair" hypothesis-and, by extension, despair more broadly-asking whether trends are consistent or inconsistent with this theory. Our work helps demonstrate that at least part of the issue lies in how these questions have been asked and, in turn, how the supporting evidence-either for or against-has been evaluated. Namely, while despair is a useful and parsimonious population health construct, this does not mean that it is easy to capture in available data, nor should we expect an unambiguous answer as to whether it is at the heart of various health behaviors and outcomes, or trends and patterns therein. By employing a more flexible measurement and modeling strategy, we shed light on this ambiguity in despair, and hopefully demonstrate that its existence and explanatory power is not a binary proposition. Indeed, while overall despair is not equally implicated in all self-destructive or harmful behaviors, elements of despair are at play across all outcomes-speaking to the utility of a more nuanced understanding of despair as a multi-dimensional construct. This conceptualization of despair may not meet the desired empirical goal of identifying (and thus operationalizing) a "singular" risk factor, but it redirects attention to the important individual dimensions of despair that exhibit strong predictive associations with specific health behaviors. Thus, while unequivocal empirical support for an overarching construct of despair is lacking, we still find the concept has utility in providing a framework that can allow researchers and practitioners to identify distinctive "sets" of risk factors-indicative of forms or dimensions of despair, rather than despair as a whole-that nevertheless capture the holistic and broadly encompassing internalization and experience of hopelessness and despair across multiple indicators. Future work further developing the measurement of despair and empirically evaluating its link with self-destructive behaviors as well as mortality is needed to advance our understanding of rising midlife mortality.

Our findings have implications for understanding population health and current demographic trends in mortality and life expectancy. Taken together, our findings suggest that despair is not equally successful or important for predicting the four outcomes, lending support to the conclusion that the outcomes may not driven by the same underlying despair construct, or that different aspects or domains of despair are differentially relevant for the self-destructive behaviors examined. The antecedent behaviors implicated in the "deaths of despair" likely have distinct etiologies. Our findings challenge the value of characterizing these causes of death as "deaths of despair" and warrant greater attention to the unique determinants of each distinct cause. Future research may be well-served by examining these behaviors and causes of death individually rather than as a shared outcome. Indeed, we find that despair is most important for predicting drug use, and drug deaths were the largest contributor to rising midlife mortality, particularly among White adults (Harris et al., 2021; Masters et al., 2017a). As such, despair may be distinctly important for understanding midlife mortality patterns among this demographic group.

It is necessary to mention several limitations of our analysis. We measure here behaviors, not mortality or causes of death. This is particularly limiting for suicidal ideation, where research demonstrates that ideation does not always precede and is not always followed by completion (Klonsky et al., 2016). Future work would benefit from an examination of the complete pathway, from despair to behavior to mortality (Gutin & Gaydosh, 2025). We also restrict our analysis to respondents with complete information on all predictors across all waves of data collection. As such, our sample is over-representative of White female adults. We also include predictors from across adolescence and early adulthood, which are removed from the measurement of our outcome by at least eight years. While the life course trajectories represent a strength of our approach, we also acknowledge that despair measured more proximally may be important.

Nevertheless, our results are consistent with the idea that isolating "despair" as a key mechanism underlying these behaviors (and subsequent causes of death) may be inappropriate given the complex social, psychological, and biological etiology of these different behaviors. That is, as much as we would hope to isolate—and thus intervene on-some kind of central risk factor (or set of factors), the (unfortunate) reality is that individuals encounter a range of individual-, community-, institutional-, and structural-level risks that shape their propensity for suicide and substance use, likely operating at different temporal scales as well. The difficulty of accurately predicting these behaviors with a comprehensive set of conceptually and empirically valid indicators—as in this analysis and prior attempts (Gutin et al., 2023)—speaks to the challenge of identifying omnibus explanations for population health trends, even when they are compelling and consistent with individuals' changing social environments and experiences. This is not to suggest that exploring such broad theories of population health change is futile, but it is also a reminder that it is equally important to approach specific population health issues on an individual basis, especially if the goal is to identify appropriate and actionable interventions.

#### Appendix

See Figs. 8, 9, 10, 11, 12, 13, 14, 15, 16, and 17 and Tables 2, 3, 4, 5, and 6.



Fig. 8 Correlation between cognitive despair predictors and outcomes (subset of Fig. 1)



Fig. 9 Correlation between emotional and biosomatic despair predictors and outcomes (subset of Fig. 1)



Fig. 10 Correlation between behavioral despair predictors and outcomes (subset of Fig. 1)



Fig. 11 Correlation between DOD (prior behaviors) and clinical predictors and outcomes (subset of Fig. 1)



· Heavy drinking · Illegal drug use · Prescription drug abuse · Suicidal ideation

Fig. 12 Importance rank of cognitive despair predictors based on mean decrease in impurity for each outcome from random forest models including despair predictors (subset of Fig. 6)



Fig. 13 Importance rank of emotional and biosomatic despair predictors based on mean decrease in impurity for each outcome from random forest models including despair predictors (subset of Fig. 6)



Fig. 14 Importance rank of behavioral despair predictors based on mean decrease in impurity for each outcome from random forest models including despair predictors (subset of Fig. 6)



· Heavy drinking · Illegal drug use · Prescription drug abuse · Suicidal ideation

**Fig. 15** Importance rank of cognitive despair predictors based on absolute value of the standardized coefficient for each outcome from LASSO models including despair predictors (subset of Fig. 7)



Fig. 16 Importance rank of emotional and biosomatic despair predictors based on absolute value of the standardized coefficient for each outcome from LASSO models including despair predictors (subset of Fig. 7)



**Fig. 17** Importance rank of behavioral despair predictors based on absolute value of the standardized coefficient for each outcome from LASSO models including despair predictors (subset of Fig. 7)

Table 2         Sample descriptive	Variable	Analytic sample	Wave V full sample	
statistics	Male	41%	43%	
	White	62%	58%	
	Black	18%	20%	
	Hispanic	13%	14%	
	Asian	6%	7%	
	Other	1%	1%	
	Caregiver education			
	High school or less	43%	45%	
	Some college	30%	30%	
	College or more	27%	25%	
	Individual education			
	High school or less	18%	21%	
	Some college	42%	43%	
	College or more	40%	36%	
	<u>n=</u>	6158	12,262	

## **Table 3** Wave V clinical predictor set by outcome

Outcome	Predictors
Suicidal ideation	Friend or family suicide attempt in last year
	Friend or family death by suicide in last year
	PTSD diagnosis
	Depression diagnosis
	Anxiety diagnosis
	Heavy drinking
Heavy drinking	Ever tried to quit drinking
	Ever wanted to quit drinking
	Able to quit drinking
	Ever had a DUI
	Number of DUIs
	Convicted for DUI
	Ever had alcohol related arrest
	Number of alcohol-related arrests
	Number of alcohol-related convictions
Illegal drug use/	Ever illegally sold drugs
Prescription drug	Ever charged with marijuana related offenses
abuse	Times charged with marijuana related offenses
	Times guilty of marijuana offenses
	Times convicted or plead guilty of marijuana
	offenses
	Ever charged with other drug offenses (nar-
	cotic drugs)
	Times charged with other drug offenses
	Ever tried to cut down on marijuana use
	Ever wanted to cut down marijuana use
	Able to quit marijuana for a month

Table beha

<b>e 4</b> Prior self-destructive viors	Question	Wave I	Wave III	Wave IV
	During the past 12 months, did you ever seriously think about committing suicide?	x	x	x
	Average 15+(men)/8+(women) drinks per week in the last month	x	x	х
	Have you ever used illegal drugs?	x		
	Used illegal drugs in the last 30 days	x	x	x
	Misused prescription drugs in the last 30 days		х	X

Domain	Question	Wave I	Wave	Wave IV
Emotional	How often was the following true during the past week?			
	Could not shake off the blues	x	x	x
	Bothered by things that usually don't bother you	x	х	x
	Felt depressed	x	х	х
	Felt sad	x	х	х
	Felt too tired to do things	x	х	х
	You enjoyed life	x	х	х
	You had trouble keeping your mind on what you were doing	x	х	х
	Felt happy	x		х
	Felt fearful	x		
	It was hard to get started doing things	x		
	Felt that life is not worth living	x		
	Felt lonely	x		
	Your appetite was poor	х		
	You talked less than usual	х		
	In the past 12 months, how often have you?			
	Laughed a lot		х	
	Cried a lot		х	
	Have you ever been diagnosed with?			
	Anxiety			х
	Depression			х
	PTSD			х
	How much do you agree or disagree with the following statem	ent?		
	I have frequent mood swings			х
	I get stressed easily			х
	I get upset easily			х
	I rarely feel blue			х
	I am not easily bothered by things			х
	I often feel isolated from others			х
Cognitive	How often was the following true during the past week?			
e	You felt you were just as good as other people	х	х	х
	I feel that people dislike me	х	х	х
	You felt hopeful about the future	х		
	You thought your life had been a failure	х		
	People were unfriendly to you	х		
	How much do you agree or disagree with the following statem	ent?		
	I am doing things right		х	
	I have many good qualities		х	
	I am not interested in abstract ideas			х
	I get angry easily			х
	There is no way I can solve the problems I have		х	
	I rarely count on good things happening to me		х	
	I have difficulty understanding abstract ideas		х	
	I have little control over things that happen to me		x	
	I have little control over important things in my life		х	
	I hardly ever expect things to go my way			x

#### Table 5 Despair predictors by domain

### Table 5 (continued)

Domain	Question	Wave I	Wave III	Wave IV
	I'm always optimistic about my future			х
	Other people determine most of what I can and cannot do	х		
	There are many things that interfere with what I want to do	х		
	I don't talk a lot			х
	I don't worry about things that happened in the past		х	
	I worry about things			х
	I make a mess of things			х
	I feel others' emotions			х
	I expect more good things to happen to me than bad		х	
	I often forget to put things back in their proper place		х	
	I get chores done right away			х
	I do not have a good imagination			х
	I keep my cool			х
	I keep in the background			х
	I am the life of the party			х
	I like order			х
	I lose my temper			х
	I am not interested in other people			х
	I am not interested in other people's problems		х	
	I rarely get irritated			х
	I am relaxed most of the time			х
	I sympathize with others' feelings			х
	I talk to a lot of different people at parties			х
	I have a vivid imagination			х
	In the last 30 days, how often have you felt:			
	Difficulties are piling up so that you cannot overcome them	х		
	Confident in your ability to handle personal problems	х		
	Things are going your way			х
	You are unable to control the important things in your life	х		
	What are the chances you will be killed by age 21?	х		
	What are the chances you will live to age 35?	х	х	
	How intelligent are you?		х	х
	How attractive are you?		х	x
	How satisfied are you with your file as a whole?	X		
	How considerate are you'?		x	
	How importure are you?		X	
	How independent are you?		X	
	How self contered are you?		X	
	You like yourself just the way you are		X	
	You have a lot to be proud of		x	
	How popular are you?		X	
Rehavioral	In the past 12 months, did this happen?		л	
Denavioral	Hurt someone in a physical fight	v	v	v
	You went into a home/building to steal something	л х	л v	л v
	You got in a physical fight	X	X	X
	<u> </u>			

## Table 5 (continued)

Domain	Question	Wave I	Wave III	Wave IV
	You were part of a physical fight between two groups	х	x	x
	You damaged property that was not yours	х	х	х
	Stole something < \$50	х	х	х
	Stole something>\$50	х	х	х
	You pulled a knife/gun on someone	х	х	х
	Had a knife/gun pulled on you	х	х	х
	You were shot/stabbed	х	х	х
	You shot/stabbed someone	х	х	х
	You sold drugs	х	х	х
	You saw someone get shot/stabbed	х	х	х
	You used a weapon to threaten someone	х	х	х
	Someone cut/stabbed you	х	х	
	You were jumped	х		
	You painted graffiti	х		
	You lied about your behavior to your parents	х		
	You drove someone's car without permission	х		
	You were a public nuisance	х		
	You stole something from a store	х		
	You were beaten up		х	х
	You used someone else's credit card		х	х
	You intentionally wrote a bad check		х	х
	You bought, sold, or held stolen property		х	х
	You were the victim of a theft		х	х
	You used a weapon in a fight		х	
	Someone pulled a gun on you		х	
	Someone pulled a knife on you		х	
	You carried a gun		х	
	You were seriously injured in a physical fight	х		
	You were hit, slapped, choked, or kicked			х
	In the past 30 days, did you?			
	Use marijuana?	х	х	х
	Smoke tobacco?	х	х	х
	Carry a weapon to school?	х		
	You go out of your way to avoid dealing with problems in your life	Х	х	
	You go with your gut and don't think about the consequences	х	х	
	You live your life without much thought for the future	х	х	
	Have you ever belonged to a gang?			
	You ran away from home	х		
	You skipped school without an excuse	х		
	You were suspended from school	х		
	You were expelled from school	х		
	You own a gun		х	
	You like to take risks		х	х
	You never swear		х	
	You never take things that don't belong to you	Х		

#### Table 5 (continued)

Domain	Question	Wave	Wave	Wave
	•	Ι	III	IV
Domain Question Your beha It is impo You don't You often You are ca How impo Do you at Are you c Are you c How man Have you Have you Biosomatic Does you BMI≥30 Self-rated	Your behavior depends on how others want you to behave	х		
	Your behavior depends on how others want you to behave It is important to fit in to the group You don't follow the crowd You often say bad things behind friends' backs You are careful How important is religion to you? Do you attend religious services? Are you currently or ever married? Are you currently or ever married? How many close friends do you have? Have you ever been arrested? Have you ever been convicted of a crime?		х	
	You don't follow the crowd		х	
	You often say bad things behind friends' backs	х		
	You are careful		х	
	How important is religion to you?	х	х	x
	Do you attend religious services?	х	х	x
	Are you currently or ever married?		х	x
	Are you currently working?		х	х
	How many close friends do you have?			х
	Have you ever been arrested?			х
	Have you ever been convicted of a crime?			x
	Have you ever been to prison?			x
Biosomatic	Does your health limit your moderate activity?		х	
	Does your health limit your ability to climb stairs?		х	
	BMI≥30	х	х	х
	Self-rated health	х	х	х

Table 6 Average importance rank by domain

Domain	Heavy drinking		Illegal drug use		Prescription drug abuse		Suicidal ideation	
	RF	LASSO	RF	LASSO	RF	LASSO	RF	LASSO
Cognitive	79.4	105.2	92.8	120.6	81.3	121.7	75.7	115.6
Emotional	119.2	137.6	124.2	108.9	97.1	112.9	76.6	102.8
Biosomatic	131.3	109.3	138.3	101.1	83.8	110.4	141.1	101.9
Behavioral	127.0	109.9	115.4	110.6	136.0	104.2	143.5	114.5
Demographic	109.8	24.3	149.5	67.3	153.3	162.0	128.8	100.5

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**Data Availability** Data from the National Longitudinal Study of Adolescent to Adult Health are available publicly through the ICPSR and under restricted-use contracts through the Carolina Population Center. More information on access to the data is available here: https://addhealth.cpc.unc.edu/data/. All code used for the analysis is available here: https://github.com/lgaydosh/despair\_ml.

#### Declarations

Conflict of interest Authors declare that they have no competing interests.

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