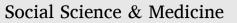
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Genetic influences on depression and selection into adverse life experiences



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ABSTRACT

Genome-wide association studies find that a large number of genetic variants jointly influence the risk of depression, which is summarized by polygenic indices (PGIs) of depressive symptoms and major depression. But PGIs by design remain agnostic about the causal mechanisms linking genes to depression. Meanwhile, the role of adverse life experiences in shaping depression risk is well-documented, including via gene-environment correlation. Building on theoretical work on dynamic and contingent genetic selection, we suggest that genetic influences may lead to differential selection into negative life experiences, forging gene-environment correlations that manifest in various permutations of depressive behaviors and environmental adversities. We also examine the extent to which apparent genetic influences may reflect spurious associations due to factors such as indirect genetic effects. Using data from two large surveys of middle-aged and older US adults, we investigate to what extent a PGI of depression predicts the risk of 27 different adversities. Further, to glean insights about the kinds of processes that might lead to gene-environment correlation, we augment these analyses with data from an original preregistered survey to measure cultural understandings of the behavioral dependence of various adversities. We find that the PGI predicts the risk of majority of adversities, net of class background and prior depression, and that the selection risk is greater for adversities typically perceived as being dependent on peoples' own behaviors. Taken together, our findings suggest that the PGI of depression largely picks up the risk of behaviorally-influenced adversities, but to a lesser degree also captures other environmental influences. The results invite further exploration into the behavioral and interactional processes that lie along the pathways intervening between genetic differences and wellbeing.

As with many diseases, the genetic architecture of depression has proven "complex": predicted by a large number of different genetic variants spread throughout the genome (Visscher et al., 2021). This complexity has prompted interest in polygenic indices (PGI), which summarize the predictive information of many thousands of variants (Mullins and Lewis, 2017; Sullivan, Daly, and O'Donovan, 2012). PGIs are deliberately agnostic about the mechanisms linking genetic variants to outcomes, and indeed pathways between specific variants and most health outcomes — including depression — remain largely mysterious (Plomin and Von Stumm, 2022). Because PGIs are strictly predictive, to whatever extent the incidence of negative life events or socially disadvantageous attributes that heighten the risk of depression are genetically influenced, these influences may also be captured in a depression PGI.

Meanwhile, numerous studies have also built a compelling case for the influence of negative life experiences on depression (e.g. Kendler et al., 2013; Kessler, 1997; Oatley and Bolton, 1985). Because few adversities are truly random, systematic influences upon the incidence of adverse experiences provide pathways leading from broader aspects of persons' lives to experiences with depression. For example, greater exposure to adversities both acute and chronic – ranging from adverse health events to family stressors and economic hardships – constitutes a core part of received explanations for the robust relationship between socioeconomic status (SES) and depression (Businelle et al., 2014; Dohrenwend and Dohrenwend, 1969).

Genes and environmental experiences are still often discussed as dueling causes of mental health. Calls to move beyond such thinking have usually focused on "gene-environment interactions", or ways that genetic differences can exacerbate or mitigate the effects of adversities (e.g. Conley et al., 2013; Domingue et al., 2017; Kendler et al., 2013). But another way that genetic and environmental causation can be interdependent is *gene-environment correlation*, in which genetic differences are implicated in the selection of individuals into different environments. The possibility of gene-environment correlation (rGE) connects to important recent developments in work on the genetics of

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depression. For example, some recent studies have examined how particular negative experiences – specifically, alcohol dependence and incarceration – are both linked to a higher risk of depression and predicted by a genetic index of depression (Andersen et al., 2017; Liu et al., 2021). Twin studies have also reported substantial genetic heritabilities for life events (Bemmels et al., 2008; Plomin et al., 1990; Schnittker, 2010), making clear there is much to understand about causes of adversity.

In this article, we examine the linkages between the genetic risk of depression and a large set of negative life experiences. Simultaneously considering a broad set of adversities allows us to also examine whether relationships between genetics predictive of depression and adversities vary by how much the latter is attributable to a person's behavior as opposed to reflecting spurious pathways of association. To avoid posthoc judgements about where different types of adversities fall along some continuum of behavioral dependence, we utilize assessments by independent raters. If the relationship between genetic predictors of depression and life experiences is a matter of gene-environment correlation, we would expect that a depression PGI will be more related to experiences that are, to a greater degree, consequences of the person's own behavior and choices. Alternatively, given that PGIs are strictly predictive, it is possible that various types of adversities are similarly associated with the depression PGI regardless of their behavioral dependence, signifying the presence of mechanisms other than geneenvironment correlation. For example, it is possible that the mediation of genetic effects on depression takes place as much - or perhaps even more so - through mechanisms of family socialization, exposure to a stressful family environment, or the co-occurrence of other biological conditions, as through direct influences on the focal person's behavior.

1. Background

1.1. Adversities and genes as causes of depression

Prior literature indicates that depression onset is often a reaction to environmental stressors (e.g. Kendler, Karkowski, and Prescott, 1999a; Kessler, 1997; Oatley and Bolton, 1985). A plausible explanation why is that negative experiences may trigger feelings or behaviors that outlast the event. For instance, stressful experiences might "teach" depressive behavior (Beck, 1967; Maier and Seligman 1976), generate lasting feelings of insecurity (Knabe and Ratzel, 2011), and overwhelm coping resources (Dohrenwend and Dohrenwend, 1969; Kessler and Essex, 1982). Alongside this work, studies comparing MZ (identical) and DZ (fraternal) twins report that genetic differences account for over half of the variation in depression (Kendler et al., 1993, 2006; Nes et al., 2013). Recent Genome-Wide Association Studies (GWAS) of depressive symptoms and major depressive disorder (MDD) estimate a "SNP-based heritability"- phenotypic variation explained by additive variation of common genetic variants - of up to 29 % (Als et al., 2022; Ormel et al., 2019). A prominent way of conceptualizing the integration of genetic and environmental causes is to see them as interacting: that genetic differences make some people more vulnerable to depressive episodes upon experiencing adversity, while other genetic differences promote resilience. Despite a highly mixed replication record (Border et al., 2019; Duncan and Keller, 2011) the basic idea of genetic moderation remains inviting, especially given abundant indication of heterogeneity in how similar life events seem to affect different people (Bonanno 2004; Boyce, 2019; Kendler et al., 2013).

Alongside the independent and interacting influences of genes and environments, gene-environment correlation highlights how influential events and environmental circumstances themselves have causes, which may include genetic influences. Genetically-influenced traits may influence behaviors that, in turn, select persons into different environments (active rGE) or prompt certain reactions in others (evocative rGE) (Plomin et al., 1977; Scarr and McCartney, 1983). Personality, cognitive, and dispositional traits have all been found to be partially influenced by genetic differences and to partially influence selection into adverse life experiences (Denissen et al., 2019; Magnus et al., 1993; Metts et al., 2021). It is therefore unsurprising that twin studies have documented the heritability of adversities, both in terms of specific events (e.g. divorce, Jerskey et al., 2010) and inventory counts (Bemmels et al., 2008; Plomin et al., 1990). Twin studies have also been used to try to estimate the extent to which the genetic influences involved in depression and specific adversities might emanate from the same genes, but these models involve additional assumptions and estimates have varied considerably (Boardman et al., 2011; Kendler and Karkowski-Shuman, 1997; Middeldorp et al., 2008; Schnittker, 2010).

The language of "dependent" vs. "independent" experiences has been used to characterize variation in adversities by how much they are "controllable" or due to a person's behavior (Kendler, Karkowski, and Prescott, 1999b). With twin data, multiple studies report that more dependent adversities are relatively more heritable (Kendler et al., 1999b; Plomin et al., 1990). Using GWAS information, Clarke et al. (2019) report that genes implicated in depression have greater overlap with a count of specifically *dependent* stressful events than a count of stressful events more generally. Importantly, non-genetic studies report that depressed individuals have a higher probability of experiencing dependent adversities whereas the risk of independent adversities is not associated with prior depression (Hammen, 1991; Williamson et al., 1995).

A separate possibility – also tested in this paper – is that adversities may be associated with a depression PGI simply by virtue of their cooccurrence with depression, for reasons other than actions or choices on the part of the focal person. First, the depression PGI may absorb genetic influences on physiological attributes that make people's lives harder - such as a physical disability, chronic illness, or even physical unattractiveness. Indeed, it is known that many pairs of traits are influenced by some of the same genes, a phenomenon known as "pleiotropy" (Paaby and Rockman, 2013). Second, the PGI may capture "indirect genetic effects" - the effect of the genes of a related person on the focal person's environment (Baud et al., 2022). For example, genetic influences affecting the poor health or risky behaviors of a parent may induce depression in the offspring via the family environment, while also reflecting in the child's genetic makeup. This study examines adversities spanning these various possibilities, which allows us to glean the extent to which the depression PGI captures behavioral pathways of selection as opposed to more generally reflecting social and physical disadvantages.

1.2. Co-development of adversity and depression

The etiology of depression is known to be highly heterogenous, and even clinical manifestations of depression do not appear to have any "final common pathway" (Parker, 2000). This complicates expectations about the typical temporal sequencing of various adversities and symptoms of depression. For example, while depression may be triggered by stressful life experiences, it also appears that individuals who come to be diagnosed as depressed tend to ubiquitously experience "inchoate" negative feelings for an extended period of time beforehand (Karp, 1994). Building upon theoretical work on contingent and dynamic selection (Freese, 2008; Freese and Shostak, 2009), we suggest that the development of depression may be shaped by different permutations and simultaneous causation of depressive behaviors and adversities over the life course. Of course, the set of potential pathways will also vary across various types of life experiences. In some cases, depression may co-evolve with an adversity: For example, substance abuse can both be a manifestation of an externalizing behavior that eventually leads to a stressful - and thereby depression-prone - life trajectory, or it can be a coping mechanism in response to already stressful life experiences. In yet other cases, we may expect a single straightforward pathway from adversity to depression onset, although the risk of the adversity itself may be orthogonal to genetic influences -

such as perhaps family-related stressors in childhood. Experiences also naturally vary in terms of whether they constitute discrete events or chronic life conditions. And finally, certain depressive symptoms may precede while others might follow the occurrence of a negative event.

To capture the complex etiology of depression, Freese and Baer-Bositis (2019) evoke the metaphor of a "network of problems", where each problem (an adversity or a symptom of depression) constitutes a node embedded within a network of interlinked problems, rendering redundant the idea that any of the problems are truly exogenous. Extending the network analogy, we can conceptualize depression as an emergent property of a network cluster, where the nodes of the cluster comprise of a variety of combinations of problems (cf. Symptom network perspectives, e.g., Barabási et al., 2011; Borsboom and Cramer, 2013). Our analysis pries at a series of these nodes to assess the extent to which a broad set of adversities linked with depression are predicted by genetic influences on depression. In other words, we will examine reduced-form models that gauge the relative effect of the depression PGI across a set of negative experiences, aggregating across intermediating pathways leading to those linkages. We then combine these estimates with other novel data to apprehend to what extent the environmental risks predicted by the PGI are mediated by potential environmental selection.

2. Data & methods

2.1. Data

We use data from the National Longitudinal Study of Adolescent to Adult Health (Add Health) and the Wisconsin Longitudinal Study (WLS). Both Add Health and WLS have collected genetic data for their respondents and include granular information on a series of adverse life experiences. Add Health is representative of the population who were in grades 7-12 in the United States in 1994-95 (Harris and Richard Udry, 2018). By 2023, five survey waves have been conducted. WLS is a 1/3sample of all Wisconsin high school graduates in 1957 (Hauser et al., 2020). Six rounds of surveys have been conducted by 2023, and later survey waves have also included a randomly selected sibling of the original respondent. Our estimation samples are based on participants in the last survey wave in both datasets. For Add Health, the sample includes respondents from Wave 5 (conducted 2016-18), aged between 33 and 44. A total of 12,300 respondents were interviewed in this wave, and roughly half have available genetic data. For WLS, the sample includes respondents from Wave 6 (conducted 2011-13), when the participants (including siblings) were between ages 45-92. Of the 9365 interviews in this wave, the majority have available genetic data.

The life course timings of the two surveys complement one another. Add Health participants are younger, which means that the adversities we consider were reported at an age when the respondents had entered many adult life stages (e.g., marriage, employment, parenthood) but were still sufficiently young for the sample not to have systematic biases due to differential mortality or memory loss. By contrast, WLS respondents are older, which allows us to observe more events that occur in later stages of adulthood, albeit with the caveat of attrition in both participants' memory and sample sizes. An additional advantage of using two different datasets is to gauge the reliability of our assessments for the adversities measured in both datasets (17 out of the 27 adversities that we consider).

The genetic indices used in this paper build on research conducted on European-ancestry samples, and further the set of genetic variants used in the GWAS was restricted to those that are common among individuals with European ancestries (Becker et al., 2021). Previous research shows that genetic indices based on European ancestry samples are not equally predictive for non-European ancestries (Martin et al., 2019). As such, the PGIs used in this paper were only made available for survey participants with non-Hispanic European ancestries. Our analyses are accordingly restricted to the sample with available PGIs (4282 cases in Add Health; 8037 in WLS) who were interviewed in the last survey wave. To account for spurious associations arising from remaining ancestry differences (population stratification), we control for the first 10 principal components of ancestry.

To gauge how lay persons attribute the life experiences to individual behavior, we conducted a preregistered survey of 160 US-based adults to rate the degree to which the respondents believed that a given adversity was attributable to behavior (preregistration available at: https://osf. io/qv3mn). This survey was conducted via Prolific (https://www.pro lific.co/), a crowd-working platform designed for academic research (Palan and Schitter, 2018). Further details about the survey and summary statistics on raters are available in Appendix I.

Raters were asked about the perceived behavioral dependence of 27 adverse experiences, in randomized order. To ensure that results are not biased by the peculiarities of how we phrased the question, we used two slightly different question wordings (randomized). Respondents either rated each adversity based on the degree to which they thought it "typically happens as the result of the behavior of the person experiencing the event" or "typically could be prevented if the person behaved differently." The rating scale ranged from 0 (not at all) to 10 (completely). We found no systematic differences between the wordings (Appendix I2) and responses are combined in the analyses that follow.

2.2. Measures

2.2.1. Adversities

We examine 27 adverse experiences that map on to inventories used in prior literature, including the PERI Life Events Scale (Dohrenwend et al., 1978), List of Threatening Life Experiences (Brugha et al., 1985), Adverse Childhood Experiences inventory (Felitti et al., 1998), and the Stress and Adversity Inventory for Adults (Slavich and Shields, 2018). These inventories include most of the adversities we consider, including network events (e.g., death or negative experiences of a loved one); physical violence (sexual abuse, physical abuse, and violent crime victimization); health and physical disability; and other personal experiences (unemployment, marital dissolution, incarceration, etc.). We include six additional experiences because of their documented impact on psychological well-being: obesity; abuse of pain medication; heavy alcohol use; exposure to a life-threatening natural disaster; experiencing disrespectful or insulting interactions; and being perceived as physically unattractive. Appendix A provides a list of previous research asserting that each of the adversities we consider causally affects depression. Detailed definitions of adversity measures are provided in Appendix B. We did not originally examine growing up in a single-parent household as an adversity; upon a reviewer's suggestion we have now included ancillary analyses for this adversity (Appendix G2); data on parental divorce are not available.

We included all adversities with available data for Add Health respondents in or by Wave 5 and/or for WLS respondents by Wave 6, and which were experienced by at least 1 % of the samples. Of the adversities we consider, 17 are included in both datasets, 5 are not included in Add Health, and 5 are not included in WLS. Table 1 summarizes the sample sizes and incidence rates of the adversities. The size of the estimation sample varies across adversities based on the applicable population (e. g., the analysis of unemployment only includes labor force participants; Appendix B fully describes such sample restrictions).

2.2.2. Genetic risk of depression

The standard approach to identifying multiple genetic variants affecting a trait entails conducting large sample GWAS that first tag the loci on the genome (single nucleotide polymorphisms, or SNPs) associated with a trait in a discovery sample, and then replicate the findings on independent sample(s) (Uffelmann et al., 2021). The coefficients from GWAS can then be used as additive weights to estimate the genetic risk of a trait for any given individual.

We use a PGI of depressive symptoms based on a sample of 1.3

Table 1

Frequencies of adversities.

	Add H	Iealth		WLS	
	Prop.		N	Prop.	N
Network events					
Parent death, early		0.27	3334	0.15	4119
Parent incarceration		0.16	3309	N/A	
Sibling death		0.11	3132	0.19	5448
Child's serious illness/accident		0.24	2404	0.23	6455
Child's divorce	N/A			0.47	6352
Child's death	N/A			0.13	7162
Widowhood	N/A			0.16	7438
Close friend's death, early	N/A			0.48	6400
Violent exposures					
Physical abuse, childhood		0.17	3383	0.33	6562
Sexual abuse, childhood		0.04	3378	0.07	6504
Sexual abuse, adulthood		0.13	3381	N/A	
Violent crime victimization		0.05	3323	N/A	
Partner abuse		0.13	3279	0.08	6509
Health & disability					
Cancer, ever diagnosed		0.03	3382	0.18	7705
Diabetes, ever diagnosed		0.06	3387	0.17	7701
Disability, childhood		0.05	3396	N/A	
Disability, current		0.05	3388	0.16	7128
Obesity		0.38	3368	0.39	6588
Pain medication abuse		0.07	3383	N/A	
Heavy alcohol use		0.12	3392	0.02	7669
Other personal experiences					
College dropout		0.24	2631	0.36	3942
Incarceration, ever		0.16	3395	0.03	6518
Divorce/separation, ever		0.31	2693	0.33	6834
Unemployment, middle adulthood		0.04	3000	0.03	4414
Disrespectful/insulting events		0.26	3333	0.16	6366
Natural disaster exposure, life-	N/A			0.17	6408
threatening					
Physical unattractiveness		0.08	2969	0.09	4052

Source: Add Health and WLS.

million individuals (Becker et al., 2021). This PGI uses Multi-Trait Analysis of GWAS (MTAG), a method for joint analysis of related phenotypes that enhances predictive power of any given PGI (Turley et al., 2018). To prevent overfitting, neither WLS nor Add Health respondents are included in the discovery GWAS used to compute the PGI for that sample. PGIs are transformed into *z*-scores within each dataset. Correlations between the depression PGI and depressive symptoms are .15 for Add Health and 0.12 for WLS (both p < .001).

2.2.3. Depressive symptoms

Depressive symptoms are measured from the most recent survey, i.e., Wave 5 of Add Health and Wave 6 of WLS. The surveys use different versions of the Center for Epidemiological Studies-Depression (CES-D) scale (Radloff, 1977). WLS includes the full CES-D, in which respondents are asked to list the number of days (0–7) in the previous week when they experienced each of 20 different feelings or phenomena. Add Health implemented a short version (CES-D5) that recorded the frequency of 5 feelings on a scale of 1 (rarely) to 4 (most/all of the time). Like the full CES-D, the CES-D5 has been validated across multiple populations and has high internal consistency (Perreira et al., 2005). We standardize the indices to allow comparisons across samples. WLS measures were collected for a random 80 % sub-sample of respondents. For both datasets, we have retained respondents with missing CES-D data in analyses not involving this measure.

2.2.4. Class background

We use two measures of class background: parental income in youth and the average educational attainment of both (or the available) parents. In Add Health, parents self-reported their education and income in Wave 1, when respondents were aged 12–19. In WLS, average parental income was retrospectively collected in 1966 using tax records from 1956 to 1960; respondents reported parents' education in Wave 1. Given that the WLS sample includes siblings of the original sample member, respondents' ages at the time of family income reports ranged between 4 and 46, with the average being 21 years. In Add Health, parental income and education are missing for 463 and 431 cases, respectively. The WLS has substantially more missing data on parental income (957 cases) than education (278 cases); we imputed missing income from father's occupation for individuals whose fathers were alive in 1960 (12 %).

2.3. Analytic strategy

For the adversities we examine to be plausible mediating behavioral pathways of depression, we must first establish their link with depression. As noted, prior research suggests at least an association, and often a causal effect, of these experiences on mental health. However, we also inspect whether the adversities are associated with heightened depressive symptoms in our data, using linear regression.

Next, we investigate differences in the risk of an adversity occurring using logit regressions predicting the log odds of the adversity given the PGI. PGIs only partly capture available additive variation attributable to genetic variation (Becker et al., 2021). PGI coefficients will therefore be biased towards attenuating the actual influence of additive genetic variation. To correct for this measurement error, we use the simulation extrapolation (SIMEX) method (Cook and Stefanski, 1994). This approach is suitable because of its compatibility with non-linear functions, and has been commonly used in analyses of PGIs (Conley et al., 2016; Dardani et al., 2021). A brief description of our use of SIMEX is provided in Appendix C; this includes sensitivity analyses showing the comparability of uncorrected estimates.

Because genes temporally precede the outcome and do not change, the marginal effect of the PGI is not subject to reverse causation. However, in both datasets, the depression PGI is negatively correlated with parental education (r = -0.15, p < .001 in Add Health and -0.05, p < .05 in WLS) and income (r = -0.08, p < .001 and -0.02, p = .07). These associations are perhaps due to adverse implications of depression in attainments in the parental generation or earlier. We control for both, assuming that, for most outcomes, these characteristics presumably preceded the adversity and that children's PGI does not typically influence parental SES. In addition, we control for sex, age, and the first 10 principal components of ancestry (Becker et al., 2021). We interpret the logit coefficient of the PGI as indicating the conditional effect of the genetic burden of depression on selection into the adversity.

Despite controls for family SES, a concern with interpreting PGI effects as "causal" is that the PGI itself may be subsuming indirect genetic influences from family members. That is, genes expressed in a parent may influence traits in the child via the family environment and socialization. In addition, a spurious correlation between the PGI and adversities may also arise from potential clustering of genetic variants within disadvantaged neighborhoods, that may persist even after adjusting for family SES and genetic ancestry. Indeed, previous research shows that heritability estimates tend to decrease in within-sibling GWAS (Howe et al., 2022). In ancillary analyses, we also include sibling fixed effects (FE), to estimate the effect of the PGI net of shared environment between siblings. The FE analyses require having genotyped siblings in the sample, which leads to considerable loss of sample size, especially in Add Health, reducing statistical power. And due to incompatibility with the SIMEX program, FE models are not corrected for measurement error in the PGI, attenuating coefficients (Angrist and Pischke, 2009:225-26). Additionally, Add Health has some discrepant reports of parent death and incarceration between full siblings. These issues limit our ability to detect significant differences in FE models.

In many contexts involving binary outcomes, it is often more intuitive to interpret results in terms of changes in predicted probability of the outcome rather than as log odds. However, in this case, the baseline rates of adversities are heterogenous (Table 1), which has implications for meaningfully comparing the effect of the PGI across adversities. If a standard deviation increase in the PGI doubles the odds of a rare event, the predicted change in probability will be smaller than doubling the odds of a common event. Given our interest in the *relative* effect of the PGI on the risk of various types of adversities, we examine changes in log odds.

To investigate whether genetic influences systematically vary for adverse experiences that may be considered behaviorally dependent, we examine the association between the effects of the depression PGI on adversities and behavioral attribution ratings from the Prolific survey. For adversities measured in both datasets, we combine the logit coefficients using inverse variance weighting to account for differing uncertainty in estimates. We preregistered the Prolific survey and our analysis plan for combining Prolific data with estimates from Add Health and WLS.

Neither dataset provides consistent leverage about the timing of adversities nor includes frequent CES-D measures, which precludes fully identifying the temporal sequencing of depression and adversities. In exploratory analyses, we draw on tools of causal mediation to decompose the conditional association between the PGI and an outcome into a mediated effect explained by the intervening variable and a residual effect capturing all other pathways (Imai et al., 2011). This allows us to assess the plausibility of the theorized pathways by interrogating whether these are consistent with the data at hand. Appendix J details measures and methods used in these analyses.

3. Results

3.1. Association between adversities and depressive symptoms

We begin by investigating how the incidence of the adversities relate to depressive symptoms. Fig. 1 summarizes conditional estimates for differences in current depressive symptoms between individuals who experienced a given adversity, versus those who were at risk but did not experience the event (Appendix D provides full regression results).

Most outcomes are significantly associated with more depressive symptoms. In general, estimates were smaller for events that may have occurred some time ago (e.g., a death in the family) versus those that are ongoing or more recent (e.g., current joblessness or violent crime victimization within the past year), which is consistent with the effect of discrete events waning with time. However, this is not always the case: for example, having ever been incarcerated has a large association with depressive symptoms, whereas a child's divorce has a weaker association. We did not find significant associations for two adversities that were measured in a single dataset (early death of a friend and childhood disability); we have retained these in our analysis to remain consistent with our initial analysis plan.

In ancillary analyses (Appendix E), we also found significant associations between the incidence of adversities and ever having experienced depressive episodes (WLS) or having been diagnosed with depression (Add Health). While absence of a diagnosis does not imply the absence of depression, the supplementary analyses bolster evidence of a positive link between adversities and depression in both datasets.

3.2. Is there evidence of gene-environment correlation?

We turn next to the relationship between adversities and the latent genetic risk of depression. Fig. 2 summarizes results of logit regressions predicting the effect of the PGI on the probability of a given adversity, conditional on covariates (full results in Appendix F). The average coefficient for the adversities observed in Add Health is higher than that of WLS (.29 vs0.17). Nevertheless, relative effects for adversities shared between the two datasets are quite consistent, with a beta-beta correlation of 0.77 (p < .001). The coefficients are also all in the expected direction, except for one adversity in WLS. Ancillary analyses stratified by sex have comparable results (Appendix tables F3-F6).

Most PGI coefficients are statistically significant (15 out of 22 in Add Health; 12 of 22 in WLS). Null results are largely consistent: in both datasets, the PGI had no effect on physical unattractiveness, sibling death, cancer, and heavy alcohol use. Inconsistencies between samples (namely, unemployment, childhood sexual abuse, and parent death) have viable explanations: Unemployment and childhood sexual abuse are relatively rare, with correspondingly wider confidence intervals; the magnitude of the childhood sexual abuse estimate is similar across samples, as is the relative rank of the PGI coefficient for unemployment. In case of parent death, the inconsistency potentially stems from different variable definitions: Add Health includes non-parental guardians whereas WLS only includes parents. A restricted definition of parent

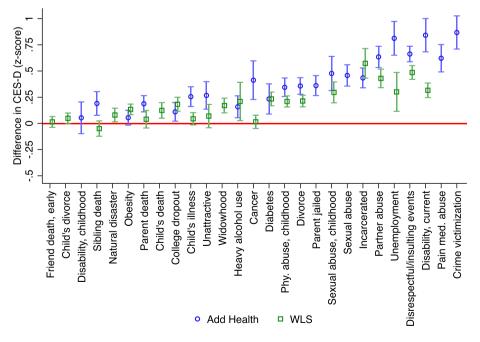


Fig. 1. Differences in Depressive Symptoms by Adversity Occurence

Note: Bars indicate 95 % confidence intervals. Models control for gender, age, 10 ancestry PCs, and class background. Source: Add Health and WLS.

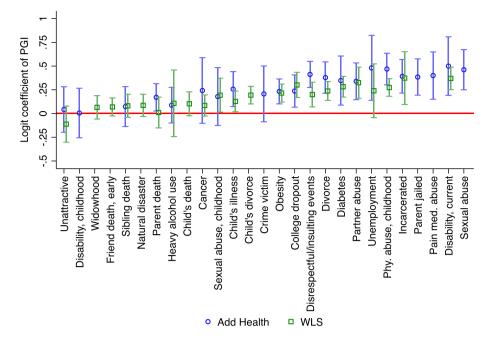


Fig. 2. Logit Estimates of the Effect of Depression PGI on Probability of Adversity

Note: Bars indicate 95 % confidence intervals. Models control for gender, age, 10 ancestry PCs, and class background. Estimates are unweighted and corrected for measurement error using SIMEX.

death in Add Health yields results consistent with WLS (Appendix G1).

Many of the significant results concur with expectations based on prior research. To give some examples: Prior twin research finds convincing evidence of heritability of marital dissolution (Jerskey et al., 2010). For unemployment, previous research has pointed to the aspects of "discipline and temperament" that predict getting laid-off (not to mention fired) as also being risk factors for divorce (Charles and Stephens, 2004). The same can be said for incarceration and depression risk (Liu et al., 2021). For experiences of being insulted/disrespected, research has found a higher tendency among depressive individuals to negatively interpret neutral or ambiguous stimuli (Everaert et al., 2018; Hindash and Amir, 2012).

However, previous scholarship is not as helpful in understanding the significant effect of the depression PGI on physical and sexual abuse and partner violence, which may be reasonably regarded as outside of a person's control. At least for childhood events, one explanation could be indirect genetic effects, as discussed above. Such indirect effects could operate by, for instance, shaping the risk of selection into unhealthy relationships or risk-taking behavior. In other cases, the PGI could simply be capturing parental genetic influences on the family environment: for instance, supplementary analyses find that growing up in a single-parent household is also predicted by the depression PGI in Add Health (Appendix G2).

In ancillary analyses, we estimated sibling FE models to net out indirect genetic effects (Appendix H). As noted, these results have diminished statistical power, especially for Add Health. Nevertheless, overall, we found significant within-sibling effects for 10 of the 12 adversities in WLS that were also significantly predicted by the PGI in the main analyses, and for 5 of 15 adversities in Add Health. Yet, consistent with the interpretation of indirect genetic effects being captured by the PGI, we find that FE estimates were not significant for child or adult sexual abuse in either dataset and for partner abuse in WLS. But, perhaps surprisingly, FE models continued to show a significant effect of the PGI on childhood physical abuse (both datasets) and for partner abuse in Add Health.

The analyses in Fig. 2 control for parental education and income. For most adversities at least one of these indicators has significant

conditional effects. Indeed, the depression PGI has no significant association with sibling death, childhood disability, and being perceived as physically unattractive, but class background does. In other cases, estimates for class are comparatively small: in particular, child's illness is significantly predicted by the PGI but not by indicators of class background. Unsurprisingly, then, the relative importance of genetic and environmental influences varies across types of adversities. The effect of sex on adversity risk also varies in direction and magnitude, as one would expect. Taken together, these results suggest that the depression PGI predicts selection into adversities through mechanisms that are not subsumed by some of the key observable dimensions of disadvantage, including class background and sex.

3.3. Does gene-environment correlation correspond with perceptions of behavioral dependence?

We now turn to the ratings of behavioral dependence of adversities. Overall, there was high inter-rater reliability across adversities (see Appendix Fig. 13). Attribution ratings were generally lower for adversities that happen to family members or friends, result from the violence of another person or external factors, or may be perceived as inborn physiological characteristics; whereas events occurring later in life and pertaining to one's own health, career, or relationships were viewed as more behaviorally dependent.

Fig. 3 plots the weighted average logit coefficients of the depression PGI against the average ratings of behavioral attribution. The linear fit line indicates a positive correlation between the behavioral attribution ratings and the coefficients of the depression PGI (r = 0.33, p = .09). This statistic does not meet the conventional significance threshold of 0.05, but given the small N (27), this remains suggestive evidence that the genetic burden of depression is more strongly associated with adversities regarded as being influenced by a person's behavior. The adversities in the top-right quadrant of the graph may be especially likely to reflect events/experiences that are notable pathways of genetic selection into depression, since these are regarded as resulting from greater behavioral input. In contrast, adversities in the top-left quadrant may be reflecting indirect genetic effects or evocative selection.

Source: Add Health and WLS.

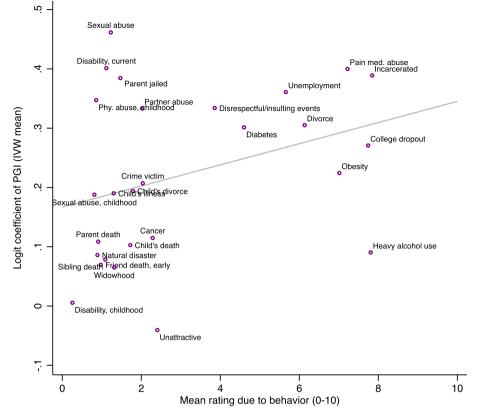


Fig. 3. Relationship between Effects of PGI on Adversity Risk and Behavioral Attribution Ratings of Adversities Note: Logit coefficients for WLS and Add Health data averaged using inverse variance weighting (IVW).

3.4. Exploratory analyses of mechanisms

In exploratory analyses, we examined three (non-mutually exclusive) possibilities connecting the depression PGI, negative life experiences, and depressive symptoms: (1) Adversities account for the association between depression PGI and current depressive symptoms; (2) Depressive symptoms immediately preceding the occurrence of adversities account for the PGI-adversity link; (3) Depression manifests early in life, and subsequently influences selection into eventual adversity. Fig. 4 summarizes the results. For legibility, we have omitted confidence intervals for statistically insignificant estimates (indicated by hollow markers) and interval bounds implying >100 % mediation.

Panel (a) shows broadly significant results consistent with mediation of the PGI-depression association by adversities. In most cases, the extent of mediation by any specific form of adversity is quite small. This is unsurprising given the sheer multiplicity of kinds of adversities one may experience; the biggest results are for disrespect, divorce, and both sexual and partner abuse. Analyses combining all adversities we consider estimate that 23 % of the association between the PGI and depressive symptoms in WLS, and 52 % in Add Health, may be mediated by these adversities.

Panels (b) and (c) show the proportion of the PGI-adversity relationship potentially explained by previous depressive symptoms. Panel (b) only includes adversities that occurred between two recent survey waves while Panel (c) only includes results for Add Health, which administered a CES-D in Wave 1. Estimates in Panel (b) show that part of the PGI-adversity association could be accounted for by depressive symptoms immediately preceding a negative experience. This could reflect anticipatory depressive symptoms in case of certain events (e.g., unemployment), but in other cases might also be suggestive of behavioral selection (e.g., pain medication abuse). Panel (c) provides evidence that genetic influence on depressive symptoms further back in time could also have shaped subsequent risk of selection into adversities. Across the analyses in panels (b) and (c), prior depression does not account for more than 10 % of the effect of the PGI on any adversity, suggesting that while depressive behaviors might sometimes lead to selection into negative experiences, the relationship between the depression PGI and the experience of adversities cannot be reduced to the behavioral consequences of antecedent depression. Finally, for some early life experiences, indirect genetic effects seem to be the only plausible explanation (e.g., parental death and incarceration).

Taken together, these analyses paint a picture of genetic influences shaping dynamic selection into both adversities and depressive symptoms over the life course, as well as to some extent passively capturing parental influences that fundamentally shape children's life experiences and future well-being.

4. Discussion

Despite its high prevalence and cost to individuals and society, much about the etiology of depression remains mysterious (Hammen, 2018; Whisman et al., 2021). Depression is demonstrably influenced by both genetic differences and adverse experiences, but how those influences fit together is one of depression's abiding puzzles. We sought to consider whether some of the observed genetic influences on depression may manifest as influences on the occurrence of adversities. That life events are heritable has been long documented in behavioral genetics (Plomin et al., 1990; Plomin and Bergeman, 1991). Building on this research and theoretical work on dynamic and contingent selection (Freese, 2008; Freese and Shostak, 2009), we suggested that genes may be responsible for behaviors that increase both the risk of certain adversities as well as the development of depression as a phenotype. We also investigated alternative pathways potentially absorbed by indices of genetic risk, such as indirect genetic effects.

We find evidence of gene-environment correlation in case of multiple adversities that are correlated with depression. Ratings from laypeople

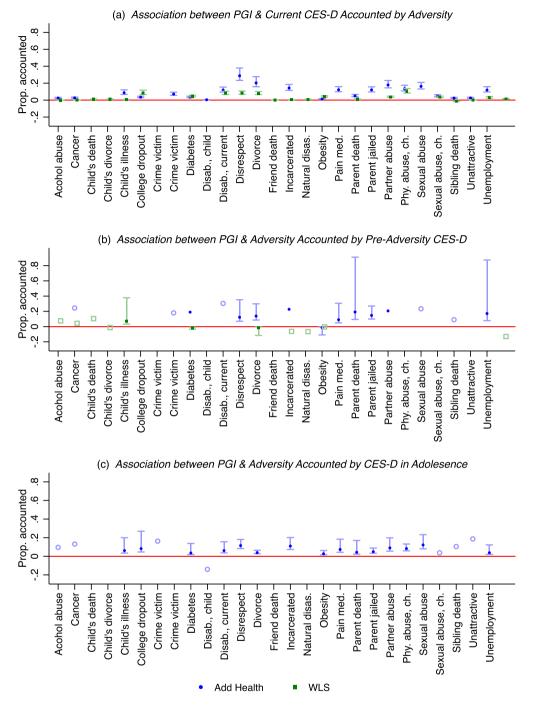


Fig. 4. Mechanisms of Association between PGI, Adversities, and Depressive Symptoms

Note: Bars indicate 95 % confidence intervals. Hollow markers indicate statistically insignificant estimates. Confidence intervals including±1 are omitted. Models control for gender, age, class background, and 10 ancestry Pcs.

Source: Add Health, WLS.

suggested that gene-environment correlations were stronger for those adversities that were considered more dependent on individuals' behaviors. However, for certain adversities, the evidence was consistent with the PGI capturing indirect genetic influences (e.g., the influence of parent genes on parent behaviors). Our analyses show that while genes significantly predicted the risk of most adversities, socioeconomic disadvantage did also, underscoring the unquestionable relevance of environmental causes even when genetic etiology is defined very broadly. These analyses have some important limitations. First, although we follow the strong scientific rationale that leads to studies using PGIs in datasets like WLS or Add Health restricting attention to Europeanancestry respondents, this creates an unfortunate, presently insuperable gap in the ability to assess how observed results may vary by ancestry, ethnicity, or race. In light of the rapid progress often associated with genetics research, headway on this front remains regrettably slow. Second, while the depression PGI is positively associated with nearly all adversities we consider, not all relationships are statistically significant. The near-uniform consistency in the direction of results suggests that many of the small, nonsignificant results may become significant with larger samples or a more predictive depression PGI than currently exists. The relative lack of precision in the current estimates also limits the effectiveness of our evaluation of whether the PGI is more strongly associated with adversities that are more behaviorally-attributed. We have treated the ratings as suggestive of relative degree of behavioral dependence between adversities, without imbuing absolute meaning to the ratings. Finally, our models imperfectly control for socioeconomic disadvantage, since parental income is measured at different points in respondents' lives. Concerns about confounding are somewhat abated by the consistency of several results in within-family models.

PGIs have become a vital product from the GWAS of complex diseases. However, not only has GWAS been more slowly successful with depression compared to many other traits, but the actual insights that GWAS results have provided in terms of elucidating causal pathways for depression have been far fewer than earlier hoped (Freese and Baer-Bositis, 2019; Ormel et al., 2019). Part of the elusiveness is due to some significant part of this genetic etiology representing different ways that genetic differences influence the relationship between depressive behaviors and the environment. This study advances our understanding of depression by illuminating some of the environmental pathways that might connect genetic influences to depression. Understanding how and why genetic differences matter encourages social scientists to think afresh about the social processes underlying inequality. Previous research has demonstrated that part of the answer may be found in expected interactions between genetic vulnerabilities and socioeconomic (dis)advantage. However, genes may also influence behaviors including use of language, perceptions, and tie formations - in profound ways. Such variations call for attention to processes of stratification that are "constructed and enacted in proximate contexts" via a range of social psychological pathways (McLeod, 2023). Our findings also have implications for research on social institutions, since individual behaviors are constrained by prevalent social rules and can only translate into particular outcomes within specific social settings (Giddens, 1984; Jepperson and Meyer, 2011). As such, even if genetic proclivities encourage certain dispositions, social meanings and interpretations are contingent upon the historical cultural setting. This idea is neatly illustrated in research by Herd et al. (2019), which demonstrates that the PGI of educational attainment has become more predictive for American women over time with the liberalization of gender norms. Others show that differences in welfare state regimes modulate the depressive effects of adversities (Levecque et al., 2011). Similarly, changes in the broader social context - including cultural understandings of mental health, medical advances, economic conditions, and institutional arrangements - can dramatically alter how genetic differences may be implicated in our well-being.

CRediT authorship contribution statement

Tamkinat Rauf: Writing – review & editing, Writing – original draft, Visualization, Validation, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. Jeremy Freese: Writing – review & editing, Writing – original draft, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Data availability

The authors will publicly share all code needed to reproduce the analyses as well as the Prolific dataset. WLS data are publicly available. Requests to access Add Health data are restricted access.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.socscimed.2024.116633.

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ONLINE SUPPLEMENT

Genetic Influences on Depression and Selection into Adverse Life Experiences

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Appendix A. Prior Research on Mental Health Effects of Adversities

In the following studies, the outcomes include mental health indices, clinical depression diagnoses, subjective well-being measures, suicidal ideation, and suicide.

Adversity	Research studies
Parent death	Cross-sectional study with matched controls (Gray et al. 2011); panel study (Moor and de Graaf 2016); event analysis of hospital admissions for depression (Berg, Rostila, and Hjern 2016)
Parent incarceration	Panel study (Gaston 2016); cross-sectional study (Turney 2021)
Sibling death	Cross-sectional study with matched controls (Bolton et al. 2016); panel study (Rostila, Saarela, and Kawachi 2013)
Child's serious illness	Meta-analysis (Cousino and Hazen 2013); cross-sectional study (Cramm and Nieboer 2011)
Child's divorce	Panel studies (Pillemer et al. 2017; Tosi and Albertini 2019)
Child death	Panel studies (Moor and de Graaf 2016; Umberson and Donnelly 2021)
Spouse death	Prospective studies (Carnelley, Wortman, and Kessler 1999; Fried et al. 2015); panel study (Lin et al. 2019)
Death of close friend, early	Cross-sectional study (Herberman Mash, Fullerton, and Ursano 2013); panel study with matched controls (Liu, Forbat, and Anderson 2019)
Violent crime victimization	Panel study with matched controls (Hochstetler et al. 2014); cross- sectional study (Cohen 2008);
Physical abuse, childhood	Effect of childhood physical abuse on adult depression in WLS (Springer et al. 2007). Meta-analysis (Lindert et al. 2014).
Sexual abuse, childhood	Meta-analyses (Lindert et al. 2014; Paolucci, Genuis, and Violato 2001)
Sexual abuse, adulthood	Meta-analysis (Chen et al. 2010); cross-sectional study (Boyle 2017)
Partner abuse	Longitudinal study (Ouellet-Morin et al. 2015); meta-analysis (Golding 1999)
Cancer	Matched controls (Binder and Coad 2013); panel study (Deimling et al. 2002)

Table A1. Research studies asserting a negative causal effect of selected adverse events and
experiences and mental health

Diabetes	Meta-analyses (Nouwen et al. 2010; Rotella and Mannucci 2013)
Disability, childhood	Panel study (Latham 2015); cross-sectional study (Ding et al. 2008)
Disability, current	Panel studies (Mandemakers and Monden 2010; Oswald and Powdthavee 2008; Turner and Noh 1988)
Obesity	Prospective study (Roberts et al. 2003); meta-analysis (Luppino et al. 2010)
Pain medication abuse	Matched controls (Scherrer et al. 2014); Mendelian Randomization (Rosoff, Davey Smith, and Lohoff 2021)
Alcohol abuse	Prospective study (Wang and Patten 2002); panel study (Aneshensel and Huba 1983)
Dropping out of college	Panel study (Liem, Lustig, and Dillon 2010); instrumental variable analysis (Oreopoulos 2007). Both examine high school dropout/completion.
Incarceration	Panel studies (Baćak, Andersen, and Schnittker 2019; Sugie and Turney 2017)
Divorce	Panel studies (Kalmijn and Monden 2006; Lin et al. 2019)
Unemployment	Panel studies (Burgard, Brand, and House 2007; Dooley, Prause, and Ham-Rowbottom 2000); national cohort study (Hakulinen et al. 2019)
Disrespectful/insulting events	Lab experiment (Sawyer et al. 2012); panel study (Finch, Kolody, and Vega 2000); cross-sectional study (Kessler, Mickelson, and Williams 1999)
Natural disaster exposure	Cross-sectional study (Moore and Friedsam 1959); meta-analyses (Beaglehole et al. 2018; Tang et al. 2014); panel study (Raker et al. 2019)
Physical unattractiveness	Cross-sectional study (Umberson and Hughes 1987); meta-analysis (Langlois et al. 2000)

Appendix B. Definition and Measurement of Adversities

1. Parent death

Add Health

At least one of the respondents' biological or social parent died by Wave 5. Derived from the following four survey questions:

- Is your biological father still alive?
- [We would like to know about the man you feel raised you. This may be a step-father, adoptive father, grandfather, etc. If you have more than one father figure, choose the one who is most important to you.] Is your father figure still alive?
- Is your biological mother still alive?
- [We would like to know about the woman you feel raised you. This may be a step-mother, adoptive mother, grandmother, etc. If you have more than one mother figure, choose the one who is most important to you.] Is your mother figure still alive?

WLS

Death of parent before age 37 (median age in Add Health W5). Derived from mother and father's year of death.

2. Parent incarceration:

Add Health

At least one of the respondents' biological or social parents was incarcerated for some time by Wave 5. Derived from the following 4 survey questions:

- Has your biological father ever spent time in jail or prison?
- [We would like to know about the man you feel raised you. This may be a step-father, adoptive father, grandfather, etc. If you have more than one father figure, choose the one who is most important to you.] Has your father figure ever spent time in jail or prison?
- Has your biological mother ever spent time in jail or prison?
- [We would like to know about the woman you feel raised you. This may be a step-mother, adoptive mother, grandmother, etc. If you have more than one mother figure, choose the one who is most important to you.] Has your mother figure ever spent time in jail or prison?

3. Sibling death

Add Health

At least one of the respondents' biological/half/step siblings had died by Wave 5. Derived from the following questions:

- *How many brothers and sisters do you have, both living and deceased?*
- How many of those [above-mentioned] siblings have died?

Legitimate skips and don't knows are coded as missing, except in cases where the respondent reported having a deceased sibling in the previous wave. The sample includes only includes respondents who had at least one sibling.

WLS

Total number of living siblings is less than total number of siblings ever born by Wave 3. Based on the following items:

- Total number of living siblings.
- Total number of siblings.

The sample only includes respondents who had at least one sibling.

4. Child's illness

Add Health

Binary indicator of whether the first 6 of the respondents' children have any of the following 15 serious disabilities or illnesses:

- Deafness
- Speech problems
- Limited sight
- Learning/developmental delay
- Chronic respiratory condition
- Chronic heart condition
- Sickle cell anemia
- Seizures
- Bone/joint problems
- Cerebral palsy
- Cystic fibrosis
- Cancer
- Hemophilia
- HIV/AIDS
- Diabetes

Although data on asthma and allergies were also collected, we excluded these conditions because of the high rate of prevalence and relatively mild nature of these conditions compared to those included above. We also excluded ADHD because it is a psychiatric condition and may have some genetic correlation with depression. This analysis only includes respondents with at least one reported child.

WLS

By Wave 6, one or more of the respondents' children had a serious illness or accident. Based on the following question:

- Has one of your children ever had a life-threatening illness or accident? This analysis only includes respondents with at least one reported child.

5. Child's divorce

WLS

By Wave 6, one or more of the respondents' children was divorced. Based on the following question:

- Has one of your children ever been divorced?

This analysis only includes respondents with at least one reported child.

6. Child death

WLS

For up to 10 children of the respondent included in the roster, whether any had died by Wave 6. Based on the question:

- Is the Participant's N-th child alive?

This analysis only includes respondents with at least one reported child.

7. Spouse death

WLS

Widowed at least once by Wave 6 vs. currently married. This measure is derived from the following variables:

- Marital history as of 2011
- Status of 197x marriage by 2011
- Status of 199x marriage by 2011
- Status of 200x marriage by 2011

This analysis only includes respondents who have ever been married.

8. Death of a close friend

WLS

Whether a close friend of the respondent died before the respondent was age 37 (median age of Add Health respondents in the last survey wave). Based on the question:

- Has a close friend ever died?

9. Violent crime victimization

Add Health

Binary indicator of whether R was a victim of (non-sexual) violent crime in the past year, in Wave 5. This variable is based on 4 questions:

- Indicate whether or not any of these things happened in the past 12 months:
 - Someone pulled a knife or gun on you.
 - Someone shot or stabbed you.
 - Someone slapped, hit, choked, or kicked you.
 - You were beaten up.

10. Physical abuse in childhood

Add Health

Binary indicator of physical abuse victimization, up till age 18, as reported in Wave 4. This variable is based on the question:

Before your 18th birthday, how often did a parent or adult caregiver hit you with a fist, kick you, or throw you down on the floor, into a wall, or down the stairs?

WLS

Binary indicator of physical abuse victimization, up till age 18, as reported in Wave 5. Based on the following questions:

- Up-until you were 18, to what extent did your father slap, shove or throw things at you?
- Up-until you were 18, to what extent did your father treat you in a way that you would now consider physical abuse?
- Up-until you were 18, to what extent did your mother slap, shove or throw things at you?
- Up-until you were 18, to what extent did your mother treat you in a way that you would now consider physical abuse?

11. Sexual abuse in childhood

Add Health

Binary indicator of sexual abuse victimization, up till age 18, as reported in Wave 4. This variable is based on the question:

- [Before your 18th birthday] How often did a parent or adult caregiver touch you in a sexual way, force you to touch him or her in a sexual way, or force you to have sexual relations?

WLS

Binary indicator of sexual abuse victimization, up till age 18, as reported in Wave 5. Based on the following questions:

- Up-until you were 18, to what extent did your father have oral, anal or vaginal sex with you against your wishes?
- Up-until you were 18, to what extent did your father use physical violence during an unwanted sexual act with you?
- Up-until you were 18, to what extent did your father treat you in a way that you would now consider sexual abuse?
- Up-until you were 18, to what extent did any other person have oral, anal or vaginal sex with you against your wishes?
- Up-until you were 18, to what extent did any other person use physical violence during an unwanted sexual act with you?
- Up-until you were 18, to what extent did any other person treat you in a way that you would now consider sexual abuse?

12. Sexual abuse in adulthood

Add Health

Binary indicator of whether respondent was ever forced into sexual activity by a non-parent/caregiver by Wave 5. Based on the question:

- Have you ever been physically forced to have any type of sexual activity against your will? Do not include any experiences with a parent or adult caregiver.

Respondents who reported having experienced sexual assault in Wave 4 were also considered positive cases.

13. Partner abuse

Add Health

Whether the respondent has been physically abused by current romantic partner in the past year. The measure is based on two survey questions (Wave 5):

- [No matter how well a couple gets along, there are times when they disagree or fight. Couples have many ways of settling their differences. Please indicate how often each of the following things has occurred in your relationship. If the length of this relationship is less than 12 months, think of the entire length of the relationship.] In the last year of this relationship, how often did your partner push or shove you, or throw something at you that could hurt? [If respondent said this did not happen in past 12 months but did happen before then, it is considered a positive response.]
- In the last year of this relationship, how often did your partner slap, hit or kick you? [If respondent said this did not happen in past 12 months but did happen before then, it is considered a positive response.]

The analysis is restricted to respondents who had a romantic partner in Wave 5.

WLS

Binary indicator of whether the respondent has ever been physically abused by a romantic partner by Wave 6. Based on the following question:

- Has your spouse or partner ever treated you in a way that some would think of as physical abuse?

14. Cancer:

Add Health

Whether the respondent has ever been diagnosed with cancer by Wave 5. Based on the following question:

- Has a doctor, nurse, or other health care provider ever told you that you have or had cancer or lymphoma or leukemia (do not include skin cancer, except melanoma)?

Respondents who reported being diagnosed in waves 3 or 4 are also considered positive cases.

WLS

Whether the respondent has ever been diagnosed with cancer by Wave 6. Based on the following question:

- Has a doctor ever told Participant they have cancer or a malignant tumor, not including minor skin cancers?

15. Diabetes:

Add Health

Whether the respondent has ever been diagnosed with diabetes (excluding those diagnosed during pregnancy) by Wave 5. Based on the following question:

- Has a doctor, nurse, or other health care provider ever told you that you have or had high blood sugar or diabetes [female: When you were not pregnant.]

Respondents who reported being diagnosed in waves 3 or 4 are also considered positive cases.

WLS

Whether the respondent has ever been diagnosed with diabetes by Wave 6. Based on the following question:

- Has a doctor ever told Participant they have diabetes?

16. Disability in childhood

Add Health

Whether the respondent had a permanent condition in Wave 1 that limited their physical ability. This variable is derived from the following questions:

- Do you have difficulty using your hands, arms, legs, or feet because of a permanent physical condition?
- Do you use a cane, crutches, walker, medically prescribed shoes, wheelchair, or scooter to get around because of a permanent physical condition?
- Do you use a brace for your hand, arm, leg, or foot because of a permanent physical condition?

17. Disability, current

Add Health

Whether or not the respondent is limited "a lot" in climbing several flights of stairs vs. "a little"/ "not limited". Based on the following question in Wave 5:

- How much does your health now limit you in climbing several flights of stairs?

WLS

The respondent has a disability that limited their activity. Derived from the following questions in Wave 4:

- Does respondent have any long-term physical or mental condition, illness or disability which limits what he/she is able to do, or which is likely to limit his/her activities in the future?
- What is respondent's most serious limiting condition?

We excluded those who reported depression, anxiety, or emotional/psychological problems as the most serious limiting condition.

18. Obesity

Add Health

The respondents' BMI was \geq 30 in Wave 5. This measure was derived from weight and height variables.

WLS

The respondents' BMI was \geq 30 in Wave 6. This measure was derived from weight and height variables.

19. Pain medication abuse

Add Health

During past month, the respondent took unprescribed pain medication in Wave 5. This measure is based on the following survey question:

In the past 30 days, which of the following types of prescription drugs have you taken that were not prescribed for you, taken in larger amounts than prescribed, more often than prescribed, for longer periods than prescribed, or that you took only for the feeling or experience they caused? Pain killers or opioids, such as Vicodin, OxyContin, Percocet, Demerol, Percodan, or Tylenol with codeine.

20. Alcohol abuse

We use here the definition of "heavy alcohol use" as 5+ incidences of binge drinking in the past month, where binge drinking is defined as having 4+ drinks on a single occasion for women and having 5+ drinks on one occasion for men (SAMHSA 2022). This definition differs from diagnostic criteria for "alcohol use disorder", which also takes into consideration alcohol-related consequences for the individual (Kranzler and Soyka 2018). Given that our definition is more expansive, we may be including cases that do not necessarily suffer from alcohol dependence. Due to data limitations, we cannot also examine alcohol use disorder.

Add Health

In Wave 5, on 5+ occasions during the past month, the respondent had 5+ drinks (4+ for women) per occasion. Constructed from multiple survey questions.

WLS

In Wave 6, on 5+ occasions during the past month, the respondent had 5+ drinks per occasion (men and women were asked the same question). Constructed from multiple survey questions.

21. College dropout

Add Health

By Wave 5, the respondent has some post-high school education, but no post-high school degree. Based on the following questions:

- What is the highest level of education that you have achieved to date?
- Are you currently attending a college, university, vocational/technical school where you take courses for academic credit?

This analysis excludes respondents who are currently enrolled and do not already have a college degree.

WLS

By Wave 4, the respondent had some post-high school education, but no post-high school degree. Based on the following items:

- Summary of ever attended college.
- Level of highest degree since high school.

We used Wave 4 data for this variable because education is unlikely to increase for any substantial number of participants after this point in the life course.

22. Incarceration:

Add Health

Whether the respondent was ever incarcerated by Wave 5. Based on the following question:

- Have you ever served time in jail, prison, juvenile detention center, or other correctional facility?

Legitimate skips were coded as didn't go to prison; non-response was coded as missing data. Respondents who reported being incarcerated in Wave 4 were considered positive cases.

WLS

Whether the respondent was ever incarcerated by Wave 6. Based on the following question:

- Have you ever been incarcerated?

23. Divorce/separation

Add Health

Indicates whether the respondent was divorced, separated, or ever divorced, vs. married in Wave 5. This variable is derived from the following survey questions:

- Are you currently married, widowed, divorced, separated?
- How many different persons have you ever married? Be sure to include your current spouse if you are married now. If you have never been married, enter 0.

We assumed that those who were currently married and reported having married more than once were previously divorced. While some of the previous marriages may have ended in widowhood, the proportion of widows is likely to be small because this is a young sample. This analysis only includes respondents who were ever married.

WLS

Divorced or separated at least once by Wave 6 vs. currently married or widowed and never divorced/separated. This measure is derived from the following variables:

- Marital history as of 2011
- Status of 197x marriage by 2011
- Status of 199x marriage by 2011
- Status of 200x marriage by 2011

This analysis only includes respondents who were ever married.

24. Unemployment

Add Health

Whether the respondent was unemployed vs. employed at the time of interview in Wave 5. Based on the following survey questions:

- Are you currently working for pay?
- Which one of the following categories best describes what you are doing now? Respondents are considered unemployed if in response to the second question they identify themselves as unemployed, regardless of whether they are currently looking for work. This analysis excludes those who are not in the labor force.

WLS

Labor force status in Wave 3 is unemployed vs. employed. This is a constructed measure available in WLS files, which is derived from 10+ survey items. This analysis excludes those who are not in the labor force. We use Wave 3 data because this variable is not included in other waves. Mean age in Wave 3 is 36 years.

25. Disrespectful/insulting events

Add Health

Binary indicator of whether the respondent feels sometimes or often treated with less respect than others vs. rarely/never feels treated with less respect. Derived from the following question in Wave 5:

- *In your day-to-day life, how often have any of the following things happened to you?* You are treated with less courtesy or respect than other people.

WLS

Binary indicator, based on the following survey question in Wave 6:

- In the past 12 months, has anyone insulted you or put you down?

26. Natural disaster exposure

WLS

Binary indicator, based on the following survey question in Wave 6:

- Have you ever experienced a life-threatening flood, fire, storm, or some other disaster?

27. Physical unattractiveness

Add Health

Attractiveness rating by interviewers, averaged across Waves 1, 3, and 4 is below the 10th percentile.

WLS

Average attractiveness rating by independent coders, based on yearbook photos, is below the 10th percentile. Ratings were normalized within coders.

Appendix C. Measurement Error Correction

The main paper reports logit estimates based on Simulation-Extrapolation method. SIMEX operates by first creating simulated datasets with increasing additive measurement error to predict how the coefficient of interest changes with measurement error; based on this projection, it then estimates how the coefficient will change if the error was instead reduced. To implement SIMEX, we need to specify the suspected error variance in the PGI. We estimated this variance using the following expression (Conley et al. 2016):

$$Var(e) = Var(PGI) + h^2 * Var(trait)$$
 ... (C1)

The variances of the PGI and the trait are set to 1 (after standardization). h^2 is the additive SNP heritability estimate from GWAS, which here is 0.056 (Becker et al. 2021). We implement SIMEX using the Stata software developed by Hardin, Schmiediche, and Carroll (2003). We present standard errors derived from 1,000 bootstraps.

SIMEX does not permit sampling weights. In the sensitivity analysis below, we provide estimates uncorrected for measurement error. For Add Health, these estimates are also weighted and survey design-corrected. To correct for survey design, we accounted for sampling stratification region (*region*), clustered by the primary sampling unit (*psucid*), and weighted the analysis by the cross-sectional sampling weight in wave 5 (*weight_cs5*). Weights were not needed for WLS analyses. These results are largely consistent with the unweighted estimates.

Table C1. Weighted Logit Regressions of Probability of Adversity in Add Health (uncorrected for measurement error)

	Parent	Parent	Sibling	Child's	Physical	Sexual	Sexual	Crime	Partner	Cancer	Diabete	s Disabilit	yDisabilit	tyObesity	Pain	Alcohol	College	Incarcer.	Divorce	Unemp.	Disrespe	c Unattractiv
	death	jailed	death	illness	abuse, child	abuse, child	abuse	victim	abuse			, childhoo d	, current	:	med. Abuse	abuse	dropout				t	e
Depression	n																					
PGI	.06	.30***	.03	.22***	.26***	.15	.18*	.24*	.27***	.09	.24*	.02	.34**	.15**	.28**	.05	.13	.23**	.20**	.34**	.21***	.07
	(.06)	(.06)	(.09)	(.06)	(.07)	(.11)	(.08)	(.11)	(.08)	(.13)	(.11)	(.11)	(.11)	(.05)	(.10)	(.08)	(.07)	(.07)	(.06)	(.11)	(.05)	(.07)
Female	02	08	.36*	.57***	.08	1.17***	2.13***	25	27	.89**	07	.31	.03	.08	07	75***	41**	-1.40***	· .02	.40	.04	24
	(.12)	(.16)	(.17)	(.13)	(.13)	(.27)	(.19)	(.20)	(.14)	(.29)	(.21)	(.23)	(.22)	(.09)	(.18)	(.13)	(.14)	(.13)	(.10)	(.28)	(.11)	(.16)
Age	.10**	06	.12**	.09*	.03	.08	.06	.03	01	.07	01	.10*	.04	.04	03	.01	.01	.04	.15***	08	.01	03
Avg. parent ed.	(.03)	(.04)	(.04)	(.03)	(.03)	(.06)	(.03)	(.06)	(.03)	(.06)	(.05)	(.05)	(.05)	(.03)	(.05)	(.04)	(.04)	(.03)	(.03)	(.06)	(.03)	(.05)
(SD)	15*	24**	37***	.01	09	08	13	18	08	.03	15	.30*	16	19**	25*	.05	40***	23**	21**	36**	10	22*
Parent	(.07)	(.08)	(.08)	(.07)	(.07)	(.12)	(.07)	(.14)	(.08)	(.14)	(.13)	(.12)	(.11)	(.06)	(.10)	(.07)	(.08)	(.08)	(.06)	(.13)	(.06)	(.11)
(SD)	52**	89***	12	.04	36**	51	22	07	.02	28	09	49*	26	18	15	.11	41**	50**	27*	.03	29**	26
	(.16)	(.18)	(.15)	(.08)	(.13)	(.29)	(.13)	(.16)	(.08)	(.20)	(.22)	(.24)	(.24)	(.11)	(.15)	(.07)	(.12)	(.18)	(.13)	(.13)	(.10)	(.14)
Constant	-4.74**	* .16	-7.07***	* -4.79**	* -2.78*	-6.84**	-5.54***	* -4.05	-1.43	-6.72**	-2.50	-7.10***	* -4.71*	-2.11*	-1.44	-2.17	-1.20	-2.60*	-6.24***	*27	-1.30	-1.40
	(1.31)	(1.33)	(1.49)	(1.32)	(1.14)	(2.27)	(1.31)	(2.41)	(1.28)	(2.49)	(1.96)	(1.84)	(2.02)	(.95)	(1.83)	(1.47)	(1.54)	(1.31)	(.99)	(2.10)	(1.21)	(1.75)
Ν	3284	3261	3082	2367	3333	3328	3330	3273	3230	3331	3336	3345	3337	3318	3333	3341	2592	3344	2659	2958	3283	2920

Uncorrected Estimates for WLS

Table C2. Logit Regressions of Probability of Adversity in WLS (uncorrected for measurement error)

	Parent	Sibling	Child's	Child's	Child's	Spouse	Friend's	Phy.	Sexual	Partner	Cancer	Diabetes	Disability	Obesity	Alcohol	College	Incarcer.	Divorce	Unemp	Disrespe	c Natura	l Unattract
	death	death	illness	divorce	death	death	death	abuse,	abuse,	abuse			, current		abuse	dropout				t	disaste	r e
								child	child													
Depression	l																					
PGI	.00	.05	.07*	.11***	.06	.03	.03	.15***	.10*	.17***	.05	.15***	.21***	.12***	.07	.17***	.21**	.13***	.13	.11**	.05	07
. 1	(.05)	(.04)	(.03)	(.03)	(.04)	(.03)	(.03)	(.03)	(.05)	(.05)	(.03)	(.03)	(.03)	(.03)	(.09)	(.03)	(.08)	(.03)	(.09)	(.04)	(.03)	(.06)
Female	.54***	.30***	.25***	.30***	.35***	1.23***	49***	40***	1.31***	1.34***	12*	48***	.04	23***	-2.58***	* .33***	-1.70***	.60***	.91***	.46***	25**	* .28*
	(.09)	(.07)	(.06)	(.05)	(.07)	(.07)	(.05)	(.05)	(.12)	(.11)	(.06)	(.06)	(.07)	(.05)	(.32)	(.07)	(.18)	(.05)	(.18)	(.07)	(.07)	(.11)
Age	05***	.03*	.04***	.09***	.08***	.13***	00	.01	06***	04***	.05***	.03***	.04***	02***	07***	.01	07***	.03***	02	07***	.00	.07
AVg.	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.02)	(.01)	(.02)	(.01)	(.04)	(.01)	(.01)	(.06)
arent ed. SD)	06	25***	05	18***	11**	07	05	07*	08	.04	.03	11**	09*	13***	12	29***	.02	.03	13	.04	.01	16*
arent	(.05)	(.04)	(.03)	(.03)	(.04)	(.04)	(.03)	(.03)	(.06)	(.05)	(.03)	(.03)	(.04)	(.03)	(.10)	(.04)	(.08)	(.03)	(.10)	(.04)	(.04)	(.06)
ncome SD)	00	15**	.04	.05*	10*	03	04	03	.02	04	.06	08*	02	03	01	13**	05	.04	03	.06	06	34***
	(.05)	(.05)	(.03)	(.03)	(.05)	(.04)	(.03)	(.03)	(.05)	(.05)	(.03)	(.04)	(.04)	(.03)	(.10)	(.04)	(.09)	(.03)	(.12)	(.03)	(.04)	(.10)
onstant	1.53*	-4.08***	• -3.88***	* -6.31***	* -8.13***	- * 11.96***	*.25	-1.12*	.73	59	-5.27***	• -3.64***	-4.40***	1.39**	1.32	-1.35*	2.35*	-2.95***	-2.42	3.36***	-1.68*	* -7.85
	(.73)	(.98)	(.54)	(.49)	(.66)	(.67)	(.45)	(.47)	(.80)	(.75)	(.54)	(.53)	(.60)	(.44)	(1.20)	(.56)	(1.05)	(.46)	(2.60)	(.55)	(.58)	(4.28)
[4119	5448	6455	6352	7162	7438	6400	6562	6504	6509	7705	7701	7128	6588	7669	3942	6518	6834	4414	6366	6408	4052

Note: * p<0.05 ** p<0.01 *** p<0.001. SEs in parentheses.

Appendix D. OLS Regressions Predicting Depressive Symptoms (full results)

These analyses are unweighted to maintain consistency with SIMEX analyses.

Add Health

Table D1. OLS Regressions of Depressive Symptoms in Add Health

	Parent	Parent	Sibling	Child's	Phy.	Sexual	Sexual	Crime		Cancer	Diabetes	s Disabilit	y Disability	Obesity	Pain	Alcohol	U	Incarcer.	Divorce	Unemp.	Disrespec	e Unattracti
	death	jailed	death	illness	abuse, child	abuse, child	abuse	victim	abuse			, childhoo	, current		med. Abuse	abuse	dropout				t	e
Adversity					ciniu	ciniu						cilitatioo	u		Abuse							
i id verbicij	0.19***	0.36***	0.19***	0.26***	0.48***	0.34***	0.46***	0.87***	0.63***	0.41***	0.23**	0.05	0.84***	0.05	0.62***	0.16**	0.11*	0.43***	0.36***	0.81***	0.66***	0.27***
	(0.04)	(0.05)	(0.06)	(0.05)	(0.08)	(0.05)	(0.05)	(0.08)	(0.05)	(0.09)	(0.07)	(0.08)	(0.08)	(0.04)	(0.07)	(0.05)	(0.05)	(0.05)	(0.04)	(0.08)	(0.04)	(0.07)
Female	0.05	0.05	0.04	0.03	0.03	0.05	-0.02	0.06	0.06	0.04	0.05	0.05	0.05	0.05	0.05	0.07	0.02	0.12***	0.04	0.05	0.02	0.06
	(0.04)	(0.04)	(0.04)	(0.04)	(0.03)	(0.03)	(0.04)	(0.03)	(0.03)	(0.04)	(0.03)	(0.03)	(0.03)	(0.04)	(0.03)	(0.04)	(0.04)	(0.04)	(0.04)	(0.03)	(0.03)	(0.04)
Age	-0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.00	0.00	0.00	0.00	0.00
	-0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-0.00	0.00	0.00	0.00	0.00
	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)
Avg. parent ed.																						
(SD)	-0.04*	-0.03	-0.05**	-0.07**	-0.05**	-0.05**	-0.05*	-0.05*	-0.05*	-0.06**	-0.05**	-0.06**	-0.04*	-0.05**	-0.04*	-0.06**	-0.04	-0.04*	-0.04	-0.03	-0.04*	-0.06**
	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)
Parent																						
income (SD)	-0.03	-0.03	-0.03	-0.06**	-0.04*	-0.04	-0.04*	-0.04*	-0.04*	-0.04*	-0.04*	-0.04*	-0.04*	-0.04*	-0.04*	-0.04*	-0.03	-0.04	-0.04*	-0.02	-0.02	-0.03
	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)
Constant	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)
	-0.01	-0.31	-0.17	-0.25	-0.14	-0.12	-0.11	-0.08	-0.24	-0.03	-0.07	-0.07	-0.10	-0.12	-0.12	-0.08	-0.10	-0.13	-0.29	-0.25	-0.20	-0.19
	(0.36)	(0.36)	(0.36)	(0.42)	(0.35)	(0.35)	(0.35)	(0.35)	(0.35)	(0.36)	(0.36)	(0.36)	(0.35)	(0.36)	(0.35)	(0.36)	(0.39)	(0.35)	(0.38)	(0.35)	(0.34)	(0.39)
R sq.	0.02	0.03	0.01	0.03	0.02	0.03	0.03	0.04	0.05	0.02	0.01	0.01	0.04	0.01	0.04	0.01	0.01	0.03	0.04	0.04	0.09	0.02
N	3297	3271	3096	2378	3340	3344	3343	3285	3241	3345	3349	3357	3350	3329	3344	3353	2607	3356	2664	2967	3295	2934

WLS Table D2. OLS Regressions of Depressive Symptoms in WLS

	Parent	Sibling	Child's	Child's	Child's	1	Friend's	2	Sexual	Partner	Cancer	Diabetes	Disability	Obesity	Alcohol	College	Incarcer	. Divorce	Unemp	Disrespec	e Natural	Unattract
	death	death	illness	divorce	death	death	death	abuse,	abuse,	abuse			, current		abuse	dropout				t	disaster	e
Advoraity								child	child													
Adversity	.04	05	.04	.05	.12**	.17***	.01	.21***	.30***	.43***	.01	.23***	.32***	.13***	.21	.18***	.57***	.21***	.30**	.49***	.08*	.07
	(.04)	(.04)	(.03)	(.03)	(.04)	(.04)	(.03)	(.03)	(.06)	(.06)	(.03)	(.04)	(.04)	(.03)	(.11)	(.04)	(.11)	(.03)	(.11)	(.04)	(.03)	(.06)
Female	.13***	.13***	.11***	.11***	.12***	.10***	.10***	.12***	.09***	.07**	.11***	.13***	.11***	.12***	.12***	.06	.14***	.10***	.10**	.09***	.12***	.12***
	(.03)	(.03)	(.03)	(.03)	(.03)	(.03)	(.03)	(.03)	(.03)	(.02)	(.02)	(.02)	(.03)	(.03)	(.02)	(.03)	(.02)	(.03)	(.03)	(.02)	(.03)	(.03)
Age	.00	.02**	00	00	.00	.00	.00	.00	.00	.00	.00	00	.00	.00	.00	01*	00	.00	.03***	.01	00	.08***
Avg. parent	(.00)	(.01)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.01)	(.00)	(.00)	(.01)	(.00)	(.00)	(.02)
ed. (SD)	06***	06***	06***	06***	07***	07***	06***	06***	06***	06***	06***	06***	06***	05***	06***	02	06***	07***	06***	06***	06***	06***
arent incom	(.02)	(.02)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.02)	(.01)	(.01)	(.02)	(.01)	(.01)	(.02)
SD)	.00	03*	02	02	02	02	03*	02	02	02	02*	02	02	02	02	01	02	02	02	03*	02	03*
	(.02)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)
Constant	26	-1.17**	.07	.04	17	14	32	36	30	17	10	07	15	11	11	.59	10	23	-2.06***	*60*	.05	-5.65**'
	(.30)	(.39)	(.26)	(.26)	(.27)	(.26)	(.27)	(.26)	(.26)	(.26)	(.26)	(.26)	(.29)	(.26)	(.26)	(.36)	(.25)	(.27)	(.52)	(.26)	(.26)	(1.35)
R sq.	.02	.01	.01	.01	.01	.02	.01	.02	.02	.02	.01	.02	.02	.01	.01	.02	.02	.02	.02	.04	.01	.02
1	3632	4697	6291	6193	6103	6333	5729	5869	5814	6341	6566	6563	6107	6324	6536	3440	6349	5837	3792	6190	6247	3497

Appendix E. OLS Regressions Predicting Depression Incidence

The figures below summarize the coefficients from linear probability models predicting ever being diagnosed with depression (Add Health, Wave 5) or ever experiencing a depressive episode (WLS, Wave 5). These analyses are unweighted to maintain consistency with SIMEX analyses.

Table E1.

	Parent	Parent	Sibling	Child's	Phy.	Sexual	Sexual	Crime	Partner	Cancer	Diabete	s Disabili	ty Disabili	ty Obesity	Pain	Alcohol	College	Incarcer	. Divorce	Unemp.	Disrespe	c Unattracti
	death	jailed	death	illness	abuse,	abuse,	abuse	victim	abuse			, , , , ,,	, current		med.	abuse	dropout				t	e
dreamaitre					child	child						childho	bd		Abuse							
Adversity	.05**	.15***	.07**	.12***	.17***	.27***	.28***	.24***	.19***	.18***	.16***	.06	.34***	.04**	.25***	.05*	.05*	.15***	.18***	.20***	.17***	.09**
	(.02)	(.02)	(.03)	(.02)	(.02)	(.04)	(.02)	(.04)	(.02)	(.04)	(.03)	(.04)	(.04)	(.02)	(.03)	(.02)	(.02)	(.02)	(.02)	(.04)	(.02)	(.03)
emale	.14***	.14***	.15***	.16***	.14***	.13***	.10***	.15***	.15***	.14***	.14***	.14***	.14***	.15***	.14***	.15***	.13***	.17***	.14***	.15***	.14***	.15***
	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)	(.02)
lge	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00	00
	00		00	00	00	00	00	00	00	00	00	00	00	00	00	00	00		00	00	00	00
Va	(.00)	(.00)	(.00)	(.01)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)
Avg. arent ed.																						
SD)	.01	.02	.01	.00	.01	.01	.01	.01	.01	.01	.01	.01	.01	.01	.01	.01	00	.01	.02*	.02	.01	.01
	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)
arent																						
ncome SD)	00	00	00	01	00	00	01	00	00	00	00	00	00	00	00	00	.00	00	01	.00	00	00
5D)	00	00	00	01	00	00	01	00	00	00	00	00	00	00	00	00	.00	00	01	.00	00	00
	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)
Constant	.33*	.22	.37*	.29	.31	.31	.33*	.27	.26	.36*	.34*	.35*	.34*	.33*	.32*	.34*	.34	.33*	.34	.26	.28	.30
	(.16)	(.16)	(.17)	(.19)	(.16)	(.16)	(.16)	(.16)	(.16)	(.16)	(.16)	(.16)	(.16)	(.16)	(.16)	(.16)	(.18)	(.16)	(.18)	(.17)	(.16)	(.17)
sq.		. ,	· /	```	` '	· /	· /	· /	. ,	. ,	. ,	. ,	. ,	. ,	× /	× /	. ,	. ,	· /	· /	· /	. ,
	.03	.04	.03	.05	.05	.04	.07	.04	.05	.03	.03	.03	.05	.03	.05	.03	.02	.04	.06	.04	.05	.03
J	3325	3300	3124	2401	3373	3368	3371	3315	3271	3374	3380	3386	3380	3358	3374	3384	2625	3385	2687	2993	3324	2960

Table E1. OLS Regressions of Probability of Depression Diagnosis in Add Health (Wave 5)

Table E2.

Table E2. OLS Regressions of Probability of Depressive Episode in WLS (Wave 5)

	Parent death	Sibling death	Child's illness	Child's divorce	Child's death	Spouse death	Friend's death	Phy. abuse, child	Sexual abuse, child	Partner abuse	Cancer	Diabetes	Disabilit	yObesity		College dropout	Incarcer	. Divorce	Unemp	Disrespe t	c Natural disaster	Unattracti e
Adversity	.02	.02	.08***	.02	.08***	.10***	.04***	.07***	.15***	.17***	.01	.04*	.11***	.02	.06	.04*	.08*	.12***	.11*	.07***	.06***	.02
F1-	(.02)	(.02)	(.01)	(.01)	(.02)	(.02)	(.01)	(.01)	(.02)	(.02)	(.01)	(.01)	(.02)	(.01)	(.04)	(.02)	(.04)	(.01)	(.04)	(.02)	(.02)	(.03)
Female	.10***	.12***	.11***	.11***	.12***	.11***	.12***	.12***	.11***	.10***	.11***	.12***	.11***	.12***	.11***	.11***	.12***	.10***	.11***	.11***	.12***	.12***
1	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.02)	(.01)	(.01)	(.01)	(.01)	(.01)	(.02)
Age	00**	01*	01***	00**	01***	01***	00**	00**	00*	00**	01***	01***	01***	01***	01***	01**	00**	01***	01**	00*	00**	00
Avg. parent	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.01)
ed. (SD)	.00	.00	.00	00	.01	.01	.00	.01	.00	.00	.01	.01	.01	.01	.01	.00	.00	.01	00	.00	.00	.00
Parent incom	(.01) ie	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)
(SD)	00	.01	.01	.01	.01	.01	.01	.01	.01	.01	.01	.01	.01	.01	.01	00	.01	.00	.01	.01	.01	00
7	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)
Constant	.45***	.53**	.48***	.46***	.54***	.58***	.40***	.39***	.37***	.43***	.52***	.53***	.54***	.49***	.52***	.55***	.44***	.48***	.66***	.38***	.42***	.23
2.07	(.12)	(.17)	(.10)	(.10)	(.09)	(.09)	(.10)	(.10)	(.10)	(.09)	(.09)	(.09)	(.09)	(.09)	(.09)	(.12)	(.10)	(.09)	(.19)	(.10)	(.10)	(.76)
R sq.	.02	.03	.03	.03	.03	.03	.03	.03	.03	.04	.02	.03	.03	.03	.02	.03	.03	.04	.03	.03	.03	.02
N	3205	3965	4719	4657	5169	5372	4788	4910	4874	4770	5562	5559	5137	4830	5544	2909	4777	4942	3203	4677	4702	2953

Appendix F. Logit Regressions Predicting Adversity Incidence

Add Health, Full Sample

Table F1. Logit Regressions of Probability of Adversity in Add Health (log odds)

	Parent	Parent	Sibling	Child's	Phy.	Sexual	Sexual	Crime	Partner	Cancer	Diabete	s Disability	/ Disability	Obesity	Pain	Alcohol	College	Incarcer	. Divorce	Unemp.	Disrespe	c Unattractiv
	death	jailed	death	illness	abuse, child	abuse, child	abuse, adult	victim	abuse			, childhood	, current		med. Abuse	abuse	dropout				t	e
PGI of																						
depression	.17*	.38***	.07	.26**	.47***	.18	.46***	.21	.34***	.24	.35**	.01	.50**	.23***	.40**	.09	.24**	.39***	.38***	.48**	.41***	.04
	(.07)	(.10)	(.11)	(.09)	(.08)	(.16)	(.11)	(.15)	(.10)	(.18)	(.13)	(.13)	(.16)	(.07)	(.13)	(.10)	(.09)	(.09)	(.08)	(.17)	(.07)	(.12)
Female	03	01	.14	.57***	06	1.17***	2.08***	19	24*	1.00***	.10	01	.13	03	.06	81***	45***	-1.29***	*.14	.21	.16*	26
	(.08)	(.10)	(.12)	(.11)	(.09)	(.21)	(.16)	(.17)	(.11)	(.23)	(.16)	(.15)	(.17)	(.08)	(.15)	(.11)	(.10)	(.11)	(.09)	(.19)	(.08)	(.14)
Age	.08***	06*	.08*	.12***	.01	04	.01	.03	03	.04	.02	.08*	.03	.03	01	.01	.04	.03	.14***	02	.01	05
Avg. parent	(.02)	(.03)	(.03)	(.03)	(.03)	(.05)	(.03)	(.05)	(.03)	(.06)	(.04)	(.04)	(.05)	(.02)	(.04)	(.03)	(.03)	(.03)	(.02)	(.04)	(.02)	(.04)
ed. (SD)	18***	35***	29***	.00	08	17	10	17	12	02	20*	.16	27**	18***	28***	.04	35***	19**	23***	30**	05	10
Parent	(.05)	(.06)	(.07)	(.05)	(.06)	(.10)	(.06)	(.11)	(.06)	(.11)	(.09)	(.09)	(.09)	(.04)	(.08)	(.06)	(.06)	(.07)	(.05)	(.11)	(.04)	(.09)
income (SD)	47**	61***	01	.02	19*	32	.07	11	01	24	10	18	27	24**	13	.07	36***	32	05	.02	18**	44**
	(.15)	(.17)	(.07)	(.06)	(.10)	(.23)	(.06)	(.19)	(.06)	(.15)	(.11)	(.16)	(.20)	(.08)	(.10)	(.05)	(.10)	(.17)	(.07)	(.23)	(.07)	(.14)
Constant	-4.12***	* .56	-5.21***	* -5.88**	* -2.01*	-2.63	-3.93**	* -4.16*	80	-5.52**	-3.48*	-5.89***	-4.36*	-1.42	-2.35	-2.20*	-2.35*	-2.11*	-6.04**		-1.53	50
	(.85)	(1.03)	(1.18)	(1.03)	(.96)	(1.73)	(1.12)	(1.83)	(1.09)	(2.11)	(1.65)	(1.48)	(1.83)	(.74)	(1.48)	(1.07)	(.99)	(.99)	(.89)	(1.67)	(.84)	(1.34)
N	3334	3309	3132	2404	3383	3378	3381	3323	3279	3382	3387	3396	3388	3368	3383	3392	2631	3395	2693	3000	3333	2969
Note: * p<0	0.05 ** p<	(0.01 ***	p<0.001	. SEs in p	arenthese	s. Unweig	ghted regi	essions.	Estimates	corrected	for meas	surement er	ror using S	SIMEX.								

WLS, Full Sample

Table F2. Logit Regressions of Probability of Adversity in WLS (log odds)

	Parent	Sibling		Child's	Child's	Spouse	Friend's	-	Sexual	Partner	Cancer	Diabetes	Disability	Obesity			Incarcer	. Divorce	Unemp	Disrespec		Unattractiv
	death	death	illness	divorce	death	death	death	abuse, child	abuse, child	abuse			, current		abuse	dropout				t	disaster	e
Depression PGI	.01	.08	.13*	.19***	.10	.07	.07	.27***	.19*	.32***	.08	.28***	.37***	.22***	.11	.30***	.37**	.24***	.24	.20**	.09	11
101	.01	.08	.15	.19	.10	.07	.07	.27	.19	.52	.08	.20	.57	.22	.11	.50	.57	.24	.24	.20	.09	11
Woman	(.08)	(.06)	(.06)	(.05)	(.06)	(.06)	(.05)	(.05)	(.09)	(.08)	(.06)	(.06)	(.06)	(.05)	(.18)	(.07)	(.14)	(.05)	(.14)	(.07)	(.06)	(.10)
Woman	.54***	.30***	.25***	.30***	.35***	1.23***	49***	40***	1.31***	1.34***	12*	48***	.04	23***	-2.58***	.33***	-1.71***	*.60***	.91***	.45***	25***	.28*
	(.09)	(.07)	(.06)	(.05)	(.07)	(.07)	(.05)	(.05)	(.12)	(.11)	(.06)	(.06)	(.07)	(.05)	(.35)	(.07)	(.19)	(.05)	(.19)	(.07)	(.07)	(.11)
Age	05***	.03*	.04***	.09***	.08***	.13***	00	.01	06***	04***	.05***	.03***	.04***	02***	07***	.01	08***	.03***	02	08***	.00	.08
	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.02)	(.01)	(.02)	(.01)	(.04)	(.01)	(.01)	(.06)
Avg. parent																						
ed. (SD)	06	25***	04	18***	10*	07	04	06*	07	.05	.03	10**	08*	13***	11	29***	.03	.04	12	.04	.01	16*
	(.05)	(.04)	(.03)	(.03)	(.04)	(.04)	(.03)	(.03)	(.06)	(.05)	(.03)	(.03)	(.04)	(.03)	(.09)	(.04)	(.08)	(.03)	(.11)	(.04)	(.04)	(.07)
Parent income (SD)																						
income (SD)	00	15*	.04	.05*	10	03	04	03	.02	04	.06	08*	02	02	01	13**	05	.04	03	.06	06	34***
~	(.05)	(.07)	(.03)	(.03)	(.06)	(.05)	(.03)	(.03)	(.07)	(.06)	(.03)	(.04)	(.03)	(.03)	(.11)	(.05)	(.07)	(.03)	(.13)	(.03)	(.04)	(.10)
Constant	1.53*	-4.07***	* -3.88***	* -6.32***	-8.12**	* -11.95***	*.26	-1.10*	.76	60	-5.27***	* -3.65***	-4.42***	1.39**	1.32	-1.41*	2.37*	-2.94***	* -2.36	3.37***	-1.68**	-7.96
	(.74)	(.96)	(.52)	(.47)	(.64)	(.68)	(.44)	(.48)	(.80)	(.72)	(.53)	(.49)	(.59)	(.43)	(1.25)	(.58)	(1.07)	(.47)	(2.77)	(.59)	(.60)	(4.45)
N	4119	5448	6455	6352	7162	7438	6400	6562	6504	6509	7705	7701	7128	6588	7669	3942	6518	6834	4414	6366	6408	4052

Add Health, Women

Table F3. Logit Regressions of Probability of Adversity in Add Health (log odds)

	Parent	Parent	Sibling	Child's	Phy.	Sexual	Sexual	Crime	Partner	Cancer	Diabete	s Disability	/ Disabilit	y Obesity	Pain	Alcohol	College	Incarcer	. Divorce	Unemp.	Disrespe	c Unattractiv
	death	jailed	death	illness	abuse, child	abuse, child	abuse, adult	victim	abuse			, childhoo	, current		med. Abuse	abuse	dropout				t	e
PGI of depression	.10	.41**	.22	.36**	.57***	.13	.37**	.27	.46**	14	.38*	.14	.61**	.21*	.18	06	.18	.42*	.38***	.53*	.41***	.10
	.10	.41**	.22	.30	.57****	.15	.57	.27	.40***	.14	.30**	.14	.01	.21**	.10	.06	.18	.42**	.30	.55*	.41****	.10
	(.10)	(.12)	(.12)	(.12)	(.14)	(.18)	(.12)	(.23)	(.15)	(.20)	(.17)	(.18)	(.23)	(.09)	(.14)	(.16)	(.11)	(.17)	(.11)	(.26)	(.10)	(.17)
Age	.06	09**	.04	.12***	.03	05	00	.03	03	.07	.03	.14*	.10	01	02	.03	00	05	.12***	03	.02	07
	(.03)	(.03)	(.05)	(.04)	(.04)	(.04)	(.03)	(.06)	(.04)	(.06)	(.06)	(.05)	(.06)	(.03)	(.05)	(.04)	(.04)	(.05)	(.03)	(.07)	(.03)	(.05)
Avg. parent																						
ed. (SD)	23**	33***	38***	.01	07	20*	09	15	10	13	34**	.22*	21	26***	34***	.02	44***	20	29***	24	07	18
Parent	(.08)	(.08)	(.10)	(.07)	(.08)	(.10)	(.06)	(.17)	(.09)	(.11)	(.12)	(.11)	(.12)	(.06)	(.10)	(.09)	(.07)	(.13)	(.07)	(.17)	(.06)	(.13)
income (SD)	39*	62***	.01	03	34*	32	.08	07	05	27	06	11	29	25*	25	.08	31*	14	.03	.07	14	73**
	(.20)	(.18)	(.07)	(.09)	(.15)	(.29)	(.06)	(.28)	(.09)	(.17)	(.13)	(.20)	(.25)	(.13)	(.15)	(.07)	(.14)	(.33)	(.07)	(.22)	(.07)	(.24)
Constant	-3.23**	1.52	-3.61*	-5.42**'	* -2.91*	-1.09	-1.28	-4.39	89	-5.62*	-3.97	-8.11***	-6.93**	25	-2.11	-3.49*	-1.29	79	-5.13**	* -2.07	-1.77	27
	(1.23)	(1.28)	(1.79)	(1.33)	(1.40)	(1.63)	(1.13)	(2.38)	(1.42)	(2.37)	(2.35)	(2.00)	(2.18)	(1.04)	(1.93)	(1.63)	(1.45)	(1.96)	(1.20)	(2.51)	(.97)	(1.96)
N	1846	1833	1744	1414	1869	1864	1868	1840	1818	1872	1872	1876	1872	1865	1870	1874	1528	1875	1522	1590	1845	1677

Add Health, Men

Table F4. Logit Regressions of Probability of Adversity in Add Health (log odds)

	Parent	Parent	Sibling	Child's	Phy.	Sexual	Sexual	Crime	Partner	Cancer	Diabete	s Disabili	y Disabilit	y Obesity	Pain	Alcohol	College	Incarcer	. Divorce	Unemp.	Disrespe	c Unattractiv
	death	jailed	death	illness	abuse, child	abuse, child	abuse, adult	victim	abuse			, childhoo	, current		med. Abuse	abuse	dropout			-	t	e
PGI of depression	.32**	.40**	11	00	.35**	.31	.93***	.15	.27*	.45	.40	18	.33	.27**	.65***	.15	.30*	.38**	.42***	.38	.42**	.01
	(.11)	(.13)	(.18)	(.16)	(.12)	(.40)	(.28)	(.24)	(.13)	(.35)	(.25)	(.22)	(.23)	(.09)	(.20)	(.13)	(.12)	(.13)	(.11)	(.26)	(.13)	(.17)
Age	.11***	03	.15**	.10	01	.03	.12	.03	02	04	01	00	08	.07*	00	.00	.09*	.05	.17***	02	00	03
	(.03)	(.04)	(.05)	(.05)	(.04)	(.13)	(.08)	.03	02	(.09)	(.07)	00	08	(.03)	(.06)	(.04)	(.04)	.03	(.04)	(.08)	(.04)	(.06)
Avg. parent	()	(.04)	(.03)	(.05)	(.04)	(.13)	(.08)	(.08)	(.04)	(.09)	(.07)	(.07)	(.07)	(.03)	(.00)	(.04)	(.04)	(.04)	(.04)	(.08)	(.04)	(.00)
ed. (SD)	10	36***	16	03	08	07	10	17	12	.32	01	.09	35*	08	22	.07	24**	18*	10	31	01	.01
Parent	(.07)	(.10)	(.11)	(.09)	(.07)	(.25)	(.22)	(.14)	(.09)	(.21)	(.15)	(.14)	(.15)	(.06)	(.13)	(.08)	(.09)	(.08)	(.07)	(.16)	(.07)	(.11)
income (SD)	59***	59*	07	.12	05	31	18	19	.03	26	17	36	31	21*	.02	.05	43**	46***	36**	45	28*	25
~	(.16)	(.25)	(.18)	(.12)	(.12)	(.50)	(.33)	(.27)	(.11)	(.40)	(.23)	(.24)	(.43)	(.08)	(.16)	(.10)	(.16)	(.13)	(.13)	(.33)	(.11)	(.16)
Constant	-5.29***	*91	-7.79***	* -5.14*	-1.22	-5.03	-8.28*	-4.28	-1.11	-2.80	-2.63	-2.98	42	-2.92**	-2.67	-1.70	-4.12**	-3.24*	-7.29**	* -2.86	-1.02	-1.32
	(1.17)	(1.56)	(1.86)	(2.03)	(1.48)	(4.82)	(3.22)	(2.86)	(1.41)	(3.61)	(2.47)	(2.55)	(2.61)	(1.06)	(2.40)	(1.65)	(1.47)	(1.45)	(1.50)	(3.04)	(1.37)	(2.09)
N	1488	1476	1388	990	1514	1514	1513	1483	1461	1510	1515	1520	1516	1503	1513	1518	1103	1520	1171	1410	1488	1292

WLS, Women

Table F5. Logit Regressions of Probability of Adversity in WLS (log odds)

	Parent	Sibling	Child's	Child's	Child's	Spouse	Friend'	s Phy.	Sexual	Partner	Cancer	Diabetes	Disability	Obesity	Alcohol	College	Incarcer	. Divorce	Unemp	Disrespec	Natural	Unattractiv
	death	death	illness	divorce	death	death	death	abuse, child	abuse, child	abuse			, current	-	abuse	dropout			-	t	disaster	e
Depression																						
PGI	.19	.16	.12	.21**	.02	.09	.03	.27***	.14	.29**	.08	.32***	.42***	.23**	27	.28**	.45	.26***	.22	.18*	.17	09
	(.12)	(.09)	(.07)	(.06)	(.08)	(.07)	(.06)	(.06)	(.12)	(.09)	(.07)	(.08)	(.08)	(.07)	(.52)	(.10)	(.31)	(.06)	(.20)	(.08)	(.09)	(.14)
Age	05***	.03	.03**	.09***	.08***	.14***	00	00	07***	04**	.04***	.04***	.04***	01	17***	.03*	13***	.04***	06	08***	.01	.19*
Aug poront	(.02)	(.02)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.05)	(.01)	(.03)	(.01)	(.06)	(.01)	(.01)	(.08)
Avg. parent ed. (SD)	06	33***	04	20***	11*	02	02	07	08	.11	.03	08	07	12**	09	26***	.01	.07*	09	02	05	30**
Parent	(.06)	(.05)	(.04)	(.04)	(.06)	(.04)	(.04)	(.04)	(.07)	(.06)	(.05)	(.05)	(.05)	(.04)	(.36)	(.06)	(.23)	(.03)	(.16)	(.05)	(.06)	(.09)
income (SD)	.02	09	.07	.03	08	08	02	05	.03	01	.06	06	.05	07	70	14*	07	.02	.03	.05	02	48***
	(.07)	(.09)	(.04)	(.04)	(.09)	(.04)	(.04)	(.04)	(.09)	(.06)	(.04)	(.05)	(.04)	(.05)	(.69)	(.07)	(.20)	(.03)	(.17)	(.04)	(.06)	(.12)
Constant	2.26*	-3.20**	-3.21***	* -6.49***	* -7.14***	* -11.31***	·31	56	2.47**	.91	-4.64***	* -4.68***	• -4.34***	.37	5.24	-2.14**	4.11*	-3.14**	* 1.18	4.39***	-2.08*	-15.66**
	(1.13)	(1.21)	(.72)	(.75)	(.91)	(.93)	(.58)	(.59)	(.88)	(.91)	(.77)	(.74)	(.77)	(.53)	(3.10)	(.73)	(2.02)	(.61)	(4.11)	(.71)	(.85)	(5.79)
N	1887	2908	3470	3411	3782	3929	3416	3541	3508	3503	4071	4069	3783	3507	4057	1901	3526	3661	1838	3408	3453	2181

WLS, Men

Table F6. Logit Regressions of Probability of Adversity in WLS (log odds)

	Paren	t Sibling	Child's	Child's	Child's	Spouse	Friend	sPhy.	Sexual	Partner	Cancer	Diabetes	s Disability	Obesity	Alcohol	College	Incarcer	.Divorce	Unemp	Disrespec	Natural	Unattractiv
	death	death	illness	divorce	death	death	death	abuse, child	abuse, child	abuse			, current		abuse	dropout				t	disaster	e
Depression PGI	21	01	.13	.17*	.27*	04	.09	.29***	.35*	.39*	.10	.24***	.31**	.20**	.14	.32***	.35*	.21**	.28	.24*	.01	24
	(.13)	(.11)	(.09)	(.07)	(.10)	(.12)	(.07)	(.07)	(.17)	(.16)	(.09)	(.07)	(.10)	(.07)	(.18)	(.09)	(.16)	(.08)	(.26)	(.11)	(.09)	(.16)
Age	- .05** *	.04*	.05***	.08***	.10***	.12***	00	.02*	04*	03	.06***	.03**	.04**	04***	06**	00	06***	.01	.05	07***	.00	08
Avg. parent ed. (SD)	. ,	(.02)	(.01)	(.01)	(.02)	(.01)	(.01)	(.01)	(.02)	(.02)	(.01)	(.01)	(.01)	(.01)	(.02)	(.01)	(.02)	(.01)	(.04)	(.01)	(.01)	(.09)
	05	15*	05	16***	09	19*	07	06	04	15	.02	12*	10	13**	11	31***	.03	01	16	.14*	.07	.02
Parent income (SD)	(.07)	(.07)	(.05)	(.04)	(.06)	(.08)	(.04)	(.04)	(.12)	(.11)	(.05)	(.05)	(.06)	(.04)	(.11)	(.05)	(.08)	(.04)	(.18)	(.06)	(.05)	(.10)
	05	23	.01	.08	13	.06	07	01	02	21	.05	10*	13*	.02	.02	11	04	.07	21	.07	12*	23
	(.07)	(.15)	(.04)	(.04)	(.08)	(.11)	(.04)	(.05)	(.18)	(.17)	(.04)	(.05)	(.06)	(.04)	(.11)	(.08)	(.07)	(.04)	(.25)	(.05)	(.06)	(.12)
Constant	1.39	-4.86**	*-4.59***	*-5.77**	*-9.05**	- *10.84***	.33	-2.09**	71	-1.50	-6.07***	*-3.25***	*-4.53***	2.27***	.51	31	1.38	-1.90**	-7.67**	2.73**	-1.54	2.84
	(.80)	(1.41)	(.86)	(.78)	(1.09)	(1.04)	(.64)	(.80)	(1.44)	(1.57)	(.73)	(.69)	(.94)	(.65)	(1.45)	(.89)	(1.21)	(.65)	(2.56)	(.92)	(.83)	(6.45)
N	2232	2540	2985	2941	3380	3509	2984	3021	2996	3006	3634	3632	3345	3081	3612	2041	2992	3173	2576	2958	2955	1871

Appendix G. Additional Analyses of Family Adversities

G1. Biological parent's death

As described in Appendix A, we used an expansive definition of parent death in the Add Health survey, including not only the death of a parent but also a parental mother or father. Our rationale for this decision was that a substantial proportion of Add Health respondents lived in diverse family arrangements, and therefore the death of a biological or legal parent alone may fail to reflect other similar experiences of the respondents who lived in other types of households. Here we show the results of ancillary analyses where we used a restricted definition of parent (biological or legal parent).

	Parent death
Depression PGI	0.14
	(0.08)
Woman	-0.00
	(0.08)
Age	0.08***
	(0.02)
Avg. parent ed. (SD)	-0.10
	(0.05)
Parent income (SD)	-0.47***
	(0.12)
Constant	-4.16***
	(0.75)
N	3292

Table G1. Logit Regressions of Probability of Parent Death in Add Health

G2. Single parent household

Our original analyses neglected to consider parental divorce or growing up in single family household as an adverse life experience. Upon a reviewer's recommendation, we also examined whether the individual grew up in single-family household. For WLS, this measure is based on a retrospective question about family structure until age 16, and in Add Health it is based on reported family structure in Wave 1. The PGI significantly predicted this adversity in the Add Health sample. In the WLS, the coefficient of the PGI was not significant, despite the larger sample size.

	(a) Add Health	(b) WLS
Depression PGI	.23*	.09
	(.11)	(.08)
Woman	37***	02
	(.10)	(.09)
Age	.04	01
	(.03)	(.02)
Avg. parent ed. (SD)	.24**	.12
	(.07)	(.06)
Parent income (SD)	-2.07***	73***
	(.22)	(.17)
Constant	-3.28**	-2.01
	(1.16)	(1.26)
Ν	2534	5815

Table G2. Logit Regressions of Probability	y of Growing up in a Single Parent Household
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Note: * p<0.05 ** p<0.01 *** p<0.001. SEs in parentheses. Estimates corrected for measurement error using SIMEX.

Appendix H. Sibling Fixed Effects

Tables H1 and H2 report sibling fixed effects estimates of the effects of the depression PGI on risk of adversities. These analyses are restricted to a sub-sample of respondents that had at least one genotyped sibling who was also included in the sample. Fixed effects estimates in the logit framework only utilize observations with within-family variation in the outcome, which can result in biased estimates (Allison 2009; Katz 2001). We used least squared models here to preserve the sample size. These analyses are not corrected for measurement error in the PGI.

Add Health

Note: Because of the small sample size, we have used a higher significance threshold in table H1 (* = p<0.10). Between full siblings, there were several discrepancies in reports of parent death and parent incarceration

	Parent	Parent	Sibling	Child's	Phy.	Sexual	Sexual	Crime	Partner	Cancer	Diabete	e Disabilit	y Disability	Obesity	y Pain	Alcoho	lCollege	e Incarce	Divorc	eUnemp	.Disres-	Unattract-
	death	jailed	death	illness			abuse,	victim	abuse		s	,	, current		med.	abuse	dropou	t.			pect	ive
					child	child	adult					childhoo	-		Abuse							
PGI of depression	03**	.03*	.01	.02	.03*	00	.01	01	.03**	00	.01	01	.01	02	.02	.01	.03	.01	.04*	00	.06***	00
	(.01)	(.02)	(.01)	(.02)	(.02)	(.01)	(.02)	(.01)	(.02)	(.01)	(.01)	(.01)	(.01)	(.02)	(.01)	(.02)	(.02)	(.02)	(.02)	(.01)	(.02)	(.01)
Female	02	.01	03	.10**	06*	.06***	.21***	00	01	.04**	.01	01	00	03	02	08**;	*04	18***	.01	.04**	.01	.01
	(.02)	(.03)	(.02)	(.05)	(.04)	(.02)	(.03)	(.02)	(.03)	(.02)	(.02)	(.02)	(.02)	(.04)	(.02)	(.03)	(.04)	(.03)	(.04)	(.02)	(.04)	(.03)
Age	.01	01	.01	.02	.02	.01**	.01	.01	.00	.00	00	01	.00	.01	.02**	01	.01	.00	.05***	01**	.00	.00
	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.00)	(.01)	(.01)	(.00)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)
Constant	.04	.41	13	49	35	50**	37	23	04	01	.08	.38*	06	.10	52**	.53*	22	.15	- 1.64***	.51** *	.07	08
	(.21)	(.30)	(.22)	(.53)	(.39)	(.22)	(.33)	(.23)	(.32)	(.18)	(.22)	(.21)	(.18)	(.47)	(.26)	(.30)	(.44)	(.35)	(.49)	(.22)	(.40)	(.28)
N	494	491	487	348	501	499	501	494	485	503	502	503	501	500	501	503	384	502	405	440	495	449

Table H1. Fixed Effects Least Squares Regressions of Probability of Adversity in Add Health

Note: * p<0.10 ** p<0.05 ** p<0.01. SEs in parentheses. Unweighted regressions.

WLS

Table H2. Fixed Effects Least Squares Regressions of Probability of Adversity in WLS

	Parent death	Sibling death		Child's divorce		Spouse death	Friend's death	s Phy. abuse, child		Partner abuse	Cancer	Diabete s	Disability , current	/ Obesity		lCollege dropou		Divorce	eUnemp	Disres- pect	Natura disaste	l Unattrac r ive
GI of epression	.00	.00	.02*	.04***	.00	.00	.01	.03**	.01	.01	.00	.02**	.04***	.03***	.00	.05***	.01*	.03***	.00	.01*	.00	01
,	(.01)	(.00)	(.01)	(.01)	(.01)	(.01)	(.01)	(.01)	(.00)	(.01)	(.01)	(.01)	(.01)	(.01)	(.00)	(.01)	(.00)	(.01)	(.00)	(.01)	(.01)	(.01)
Female	.07***	00	.05**	.05**	.04***	.14***	10***	06***	.06***	.08***	01	07***	01	04*	03***	· .07***	04***	.12***	.02**	.06***	04**	.02
	(.02)	(.00)	(.02)	(.02)	(.01)	(.01)	(.02)	(.02)	(.01)	(.01)	(.01)	(.01)	(.01)	(.02)	(.00)	(.02)	(.01)	(.02)	(.01)	(.01)	(.01)	(.01)
Age	01***	° .00	.01***	.02***	.01***	.02***	.00	.00	00***	00**	.01***	.00***	.00**	00	00**	.00	00***	.01**	00	01***	.00	.01
	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.00)	(.01)
Constant	.75***	.16***	19	90***	·48***	- * 1.00**'	*.48***	.16	.34***	.24***	27**	09	13	.58***	.12***	.30*	.22***	13	.09	.95***	.14	59
	(.12)	(.02)	(.11)	(.13)	(.08)	(.08)	(.13)	(.12)	(.07)	(.07)	(.09)	(.08)	(.09)	(.12)	(.03)	(.15)	(.05)	(.12)	(.09)	(.10)	(.10)	(.58)
1	1994	2360	3082	3036	3354	3510	3043	3110	3083	3105	3634	3632	3319	3145	3620	1957	3113	3199	1884	3032	3045	1511

Appendix I. Behavioral Attribution Ratings

I1. Overview

The survey of behavioral attribution ratings was fielded on Prolific.co in December 2022. Participants were recruited for an estimated time commitment of 5 minutes in exchange for \$1. We restricted participation to persons with a minimum approval rating of 95% on previous Prolific assignments, and with fewer than 500 past assignments on this platform (Meyers et al. 2020). Before the adversity items, raters were given an attention check and two training questions; failed attention checks led to the removal of 5 of our sex-balanced group of 160 raters.

Table I1 proves the summary statistics of key demographic measures. The average sample age was 35 (min 18, max 75). Most of the sample was fairly educated, with 46% of the participants having at least a 4-year college degree.

	Proportion
Male	0.50
Female	0.50
Age: Under 25	0.27
Age: 25-44	0.52
Age: 45-64	0.15
Age: 65+	0.06
Education: High school or less	0.21
Education: Assoc./Some college	0.34
Education: College+	0.46
Foreign born	0.09
N	155

Table I1. Descriptive Statistics of Prolific Sample

Source: Prolific survey fielded December 2022.

We randomized participants into 2 question-wording conditions, to ensure that responses are not biased by specific wording. In the first condition, respondents were asked to rate the extent to which an adversity resulted from a person's behavior (behave condition), and in the second condition participants were asked to rate the extent to which the adversity could have been prevented if the person acted differently (prevent condition). In each condition, respondents were asked to rate all 27 adversities, presented in a randomized order.

The survey instrument can be viewed at <u>https://osf.io/vp7tw/</u>. We aimed to phrase the survey items to match the descriptions of events/experiences in the Add Health and WLS samples. However, in the case of sexual abuse there is a discrepancy with how the adversity was measured in Add Health (ever being abused by persons other than primary caregivers). To create a comparable rating for this adversity, we averaged ratings for two items (sexual abuse in childhood and adulthood).

I2. Analysis of Question-wording Conditions

We used t-tests to examine whether the mean ratings vary in the two conditions. Table I2 summarizes the mean difference between prevent vs. behave conditions along with p-values for the associated t-test statistic. Based on a conventional significance threshold of p<0.05, only 9 out of the 27 tests were statistically significant. There is also no meaningful pattern in the direction of difference. Based on these results, it appears that the different question-wording conditions did not significantly affect the average ratings.

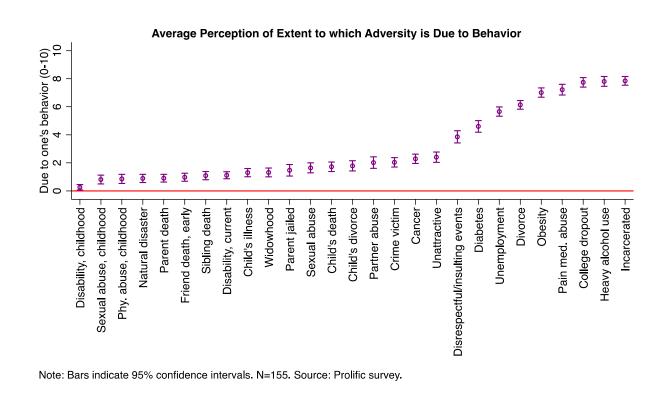
	Difference in Means	P-value
Parent death	-0.57	0.04
Parent jailed	0.50	0.24
Sibling death	-0.49	0.10
Child's illness	0.41	0.17
Child's divorce	0.42	0.26
Child's death	-0.44	0.21
Widowhood	-0.62	0.05
Friend death, early	-0.47	0.11
Phy. abuse, childhood	-0.11	0.75
Sexual abuse, childhood	0.03	0.92
Sexual abuse	0.77	0.03
Crime victim	0.18	0.60
Partner abuse	1.18	0.00
Cancer	0.49	0.15
Diabetes	1.51	0.00
Disability, childhood	-0.09	0.64
Disability, current	-0.10	0.70
Obesity	0.93	0.01
Pain med. abuse	1.04	0.01
Heavy alcohol use	0.82	0.02
College dropout	0.33	0.35
Incarcerated	0.48	0.13
Divorce	0.43	0.17
Unemployment	0.72	0.03
Disrespectful/insulting events	1.23	0.01
Natural disaster	0.06	0.84
Unattractive	0.65	0.08

Table I2. Summary of t-tests Comparing Difference in Mean Ratings Between Question-
wording Conditions

Source: Prolific survey fielded in December 2022.

I3. Average Ratings

Figure I3 summarizes the average rating of each adversity as being behaviorally dependent. The narrow confidence intervals reflect high degree of inter-rater consistency (inter-rater reliability coefficient is >.99).



Appendix J. Mechanisms of Association between PGI, Adversities, and Depression

To unpack the pathways of association, we computed the proportion of the conditional effects of the PGI on the outcome(s) that can be accounted for by the hypothesized intervening variable. This analysis draws on tools from causal mediation to decompose the "total effect" of the PGI into an "indirect effect" – or the Average Causal Mediation Effect (ACME) – and a "direct effect" capturing all other mechanisms. We used the Stata package *medeff* (Hicks and Tingley 2011). This package does not make *a priori* assumptions about the distribution of the mediation effect, but instead uses simulations to estimate standard errors, and allows for non-linear specification of the outcome and mediators. All analyses control for sex, age, and genetic ancestry PCs. These analyses are not corrected for measurement error in the PGI, which would lead to underestimation of the total effect estimates.

The decomposition estimates can be identified if conditional on covariates, the assignment of the treatment (PGI) can be considered random, and the covariates are not affected by the treatment (Imai et al. 2011). Here, the covariates are not impacted by the PGI, but we cannot be certain that conditional on the covariates the PGI is randomly distributed. We interpret these results as only suggestive of whether a theorized mechanism is plausible given the observed data.

We conducted 3 sets of analyses, as discussed in the paper. Below, we describe the additional measures involved in these analyses, followed by the results of the decomposition.

Measures

Transition into adversity

To investigate whether depressive symptoms could have led to selection into adversities, we examined a subset of adversities that occurred after depressive symptoms had been recorded in a preceding survey wave. We considered a case as having experienced transition into adversity if the respondent experienced the adversity in/by period t, but had not experienced the adversity in period t-2 or t-1. Cases that consistently reported experiencing the adversity at these time points were removed from the analysis. Cases that were at-risk but did not experience the adversity at any timepoint were considered negative cases, and were included in the analysis. Definitions of transition measures used in the analysis are listed below.

- 1. Parent death
- *Add Health:* One of the respondents' biological or social parent died by Wave 5, but none had died by Wave 4. Or, the event occurred by Wave 4 but after Wave 3.
- 2. Parent incarceration:
- *Add Health:* At least one of the respondents' biological or social parent was incarcerated by Wave 5, but none had been incarcerated by Wave 4. Or, the event occurred by Wave 4 but after Wave 3.
- 3. Sibling death
- *Add Health:* At least one of the respondents' siblings had died by Wave 5, but none of the siblings had died by Wave 4.

- 4. Child's illness
- *WLS:* At least one or more of the respondents' children had a serious illness or accident by Wave 6, but no children had serious illness/accident by Wave 5.
- 5. Child's divorce
- *WLS:* One or more of the respondents' children was divorced by Wave 6, no children had been divorced by Wave 5.
- 6. Child's death
- *WLS:* Whether any of the respondent's children had died by Wave 6, but after Wave 5. Or, the event occurred by Wave 5 but after Wave 4.
- 7. Spouse death
- *WLS:* The respondent was widowed in Wave 6, but not in Wave 5. Or, the event occurred by Wave 5 but after Wave 4.
- 8. Violent crime victimization
- *Add Health:* R was a victim of (non-sexual) violent crime in the past 12 months in Wave 5, but not in Wave 4.
- 9. Sexual abuse in adulthood
- *Add Health:* The respondent was ever forced into sexual activity (by non-parent/caregiver) by Wave 5, but after Wave 4.

10. Partner abuse

- *Add Health:* Respondent reported being physically abused by current romantic partner in Wave 5, but not in Wave 4.
- 11. Cancer
- *Add Health:* The respondent has ever been diagnosed with cancer in Wave 5 but not in Wave 4. Or, the event occurred by Wave 4 but after Wave 3.
- *WLS:* The respondent has ever been diagnosed with cancer in Wave 6, but not in Wave 5. Or, the event occurred by Wave 5, but after Wave 4.
- 12. Diabetes
- *Add Health:* The respondent has ever been diagnosed with diabetes in Wave 5 but not in Wave 4. Or, the event occurred by Wave 4 but after Wave 3.
- *WLS:* The respondent has ever been diagnosed with diabetes in Wave 6, but not in Wave 5. Or, the event occurred by Wave 5 but after Wave 4.
- 13. Disability, current
- *Add Health:* The respondent is limited "a lot" in climbing several flights of stairs in Wave 5, but not in Wave 4.

14. Obesity

- Add Health: The respondents' BMI was \geq 30 in Wave 5, but not in Wave 4. Or, the BMI was \geq 30 in Wave 4, but not in Wave 3.
- WLS: The respondents' BMI was ≥30 in Wave 6, but not in Wave 5. Or, BMI was ≥30 in Wave 5, but not in Wave 4.
- 15. Pain medication abuse
- *Add Health:* The respondent took unprescribed pain medication in Wave 5, but not in Wave 4.
- 16. Alcohol abuse
- *WLS:* In Wave 6, on 5+ occasions during the past month, the respondent had 5+ drinks per occasion (men and women were asked the same question), but not in Wave 5.
- 17. Incarceration
- Add Health: Whether the respondent was ever incarcerated by Wave 5, but after Wave 4.
- WLS: Whether the respondent was ever incarcerated by Wave 6, but after Wave 5.
- 18. Unemployment
- Add Health: Whether the respondent was unemployed in Wave 5, but not in Wave 4.
- 19. Divorce/separation
- Add Health: Divorced or separated at least once by Wave 5, but after Wave 4.
- WLS: Divorced or separated at least once by Wave 6, but after Wave 5.
- 20. Disrespectful/insulting events
- *Add Health:* The respondent feels sometimes or often treated with less respect than others versus rarely/never in Wave 5, but not in Wave 4.
- *WLS:* The respondent felt insulted or put down by others in the past year in Wave 6, but not in Wave 5.
- 21. Natural disaster exposure
- *WLS:* The respondent experienced a life-threatening flood, fire, storm, or some other disaster in Wave 6, but not in Wave 5.

Lagged CES-D

To investigate whether prior depressive symptoms mediated the link between PGI and aversity, we used CES-D scores in Wave t-1, if the adversity had occurred by Wave t but not in Wave t-1. If the adversity had occurred in Wave t-1 but not in t-2, then we used CES-D score from Wave t-2 instead. This entailed using CES-D scores from Waves 3 and 4 in Add Health and Waves 4 and 5 in WLS. All CES-D scores were standardized.

CES-D in adolescence

Add Health administered CES-D in Wave 1, when respondents were aged 12-19. This measure is used in analyses investigating mediation by early depression.

Results

Table J1 summarizes analyses decomposing the effects of the depression PGI on current CES-D into an ACME – that could be explained by the adversity – and a "direct effect" capturing all other pathways. Note that the "total effect" of PGI on CES-D varies across adversities because of differences in the underlying estimation samples.

		Add Health		WLS			
	Total effect	Direct effect	ACME	Total effect	Direct effect	ACME	
Cancer	0.137	0.133	0.004	0.118	0.118	0.00	
Child's death				0.123	0.122	0.00	
Child's divorce				0.123	0.122	0.00	
Child's illness	0.133	0.121	0.011	0.122	0.121	0.00	
College dropout	0.144	0.139	0.005	0.115	0.106	0.01	
Crime victimization	0.139	0.129	0.010				
Diabetes	0.138	0.133	0.005	0.119	0.113	0.00	
Disability, childhood	0.135	0.135	0.001				
Disability, current	0.142	0.126	0.017	0.119	0.110	0.01	
Disrespectful/insulting events	0.149	0.106	0.043	0.116	0.107	0.01	
Divorce	0.134	0.107	0.027	0.124	0.114	0.01	
Friend death, early				0.101	0.101	0.00	
Heavy alcohol use	0.137	0.133	0.003	0.117	0.117	0.00	
Incarcerated	0.144	0.123	0.021	0.118	0.118	0.00	
Natural disaster				0.119	0.118	0.00	
Obesity	0.138	0.137	0.002	0.119	0.114	0.00	
Pain med. abuse	0.140	0.123	0.017				
Parent death	0.136	0.129	0.007	0.084	0.083	0.00	
Parent jailed	0.139	0.123	0.017				
Partner abuse	0.150	0.123	0.027	0.122	0.118	0.00	
Phy. abuse, childhood	0.141	0.122	0.019	0.105	0.094	0.01	
Sexual abuse	0.144	0.120	0.023				
Sexual abuse, childhood	0.136	0.130	0.007	0.102	0.098	0.00	
Sibling death	0.138	0.135	0.003	0.101	0.102	-0.00	
Unattractive	0.143	0.139	0.004	0.099	0.099	0.00	
Unemployment	0.137	0.120	0.016	0.105	0.102	0.00	
Widowhood				0.120	0.118	0.00	

Table J1. Decomposition of Effect of PGI on CES-D

Source: Add Health and WLS.

In Table J2, we summarize analyses decomposing the effect of the PGI on adversities into an ACME that could be explained by depressive symptoms in the pre-adversity wave, and a direct effect capturing all other pathways. This analysis has two limitations: (1) the ACME could be reflecting anticipation effects of an impending negative event, rather than an effect of depressive symptoms on adversity risk. (2) The analyses suffer from sample selection bias, which may be particularly relevant for certain events. For example, positive cases of incarceration in the WLS pertain to individuals who were incarcerated for the first time in older adulthood.

		Add Health		WLS				
	Total effect	Direct effect	ACME	Total effect	Direct effect	ACME		
Cancer	0.004	0.003	0.001	0.001	0.000	0.000		
Child's death				0.006	0.005	0.00		
Child's divorce				0.009	0.009	0.000		
Child's illness				0.012	0.011	0.00		
Crime victimization	0.006	0.005	0.001					
Diabetes	0.009	0.007	0.002	0.019	0.019	0.00		
Disability, current	0.003	0.002	0.001					
Disrespectful/insulting events	0.023	0.020	0.003					
Divorce	0.032	0.027	0.005	0.013	0.013	0.00		
Heavy alcohol use				0.002	0.001	0.00		
Incarcerated	0.009	0.007	0.002	-0.001	-0.001	0.00		
Natural disaster				-0.002	-0.002	0.00		
Obesity	0.015	0.015	0.000	0.012	0.012	0.00		
Pain med. abuse	0.012	0.011	0.001					
Parent death	0.018	0.015	0.003					
Parent jailed	0.030	0.026	0.005					
Partner abuse	0.012	0.010	0.003					
Sexual abuse	0.007	0.005	0.002					
Sibling death	0.001	0.001	0.000					
Unemployment	0.009	0.008	0.002					
Widowhood				0.004	0.004	-0.00		

Table J2. Decomposition of Effect of PGI on Adversity

Source: Add Health and WLS.

Table J3 shows the decomposition of the conditional association between the PGI and adversities into ACME explained by depressive symptoms in early adulthood and a direct effect reflecting all other pathways.

	Add Health							
	Total effect	Direct effect	ACME					
Cancer	0.005	0.004	0.001					
Child's illness	0.025	0.023	0.002					
College dropout	0.023	0.021	0.002					
Crime victim	0.006	0.005	0.001					
Diabetes	0.012	0.011	0.000					
Disability, childhood	0.000	-0.001	0.001					
Disability, current	0.014	0.013	0.001					
Disrespectful/insulting events	0.046	0.041	0.005					
Divorce	0.045	0.043	0.002					
Heavy alcohol use	0.006	0.005	0.001					
Incarcerated	0.028	0.025	0.003					
Obesity	0.029	0.028	0.001					
Pain med. abuse	0.016	0.015	0.001					
Parent death	0.019	0.018	0.001					
Parent jailed	0.030	0.028	0.002					
Partner abuse	0.023	0.021	0.002					
Phy. abuse, childhood	0.040	0.037	0.004					
Sexual abuse	0.028	0.024	0.004					
Sexual abuse, childhood	0.004	0.004	0.000					
Sibling death	0.004	0.003	0.001					
Unattractive	0.002	0.001	0.001					
Unemployment	0.013	0.012	0.001					

Source: Add Health.

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