**Supplemental Table 1. Detailed descriptions of study variables**

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| --- | --- |
| **Variable** | **Description** |
| Adolescent psychopathology | Any indication of an internalizing or externalizing condition between ages 11-18. |
| Internalizing psychopathology | Internalizing psychopathology included reports of depression, anxiety, post-traumatic stress disorder (PTSD), and eating disorder. Depression was assessed via prospective and retrospective reports. Prospective depression was assessed via an 18-item version of the Center for Epidemiological Studies-Depression Scale (CES-D). Scores were pro-rated to 20 items and standard depression cut-offs of 22 and 24 were used to identify depression in males and females, respectively (Roberts, Lewinsohn, & Seeley, 1991). We used prospective assessments for participants who were 18 or younger at the time of the interview and who had non-missing information for at least five of the 18 CES-D items. Retrospective reports of depression included participants who self-reported a depression diagnosis between ages 11 and 18 and who reported a depression diagnosis two or more years following, or prior to, their first prospective assessment of depression. Retrospective reports were drawn from Wave IV when available and Wave V for those without Wave IV information. Participants with either prospective depression or retrospective reports of depression more than two years prior to, or following, the prospective assessment of depression were included in the indicator for adolescent depression. We supplemented the prospective reports of depression with retrospective information because prospectively-assessed depression considered only very recent symptoms (symptoms over the prior week). Assessments of anxiety, PTSD, and eating disorder were limited to retrospective reports of diagnosis between ages 11 and 18. Retrospective reports were assessed via the questions “Has a doctor, nurse or other health care provider ever told you that you have or had X condition?” and “How old were you when you were diagnosed by a doctor, nurse or other health care provider with X condition?” |
| Externalizing psychopathology | Externalizing psychopathology included prospective reports of conduct disorder and retrospective reports of attention-deficit hyperactivity disorder (ADHD). We assessed conduct disorder using an 11-item delinquency scale administered at Waves I and II that corresponds to the DSM-IV conduct disorder criteria, and that has been previously used in Add Health (Miles, van den Bree, & Pickens, 2002). **Supplemental Table 2** shows the questions that were used to create the indicators for the scale. Consistent with prior work (Miles et al., 2002), item responses were combined across Waves I and II. Participants with missing data across both waves for three or more indicators were coded as missing. Consistent with DSM-IV criteria, participants with three or more conduct-disorder indicators were classified as having conduct disorder. ADHD diagnoses included retrospective reports of ADHD diagnosis between ages 11 and 18. Questions used the same format as retrospective reports for internalizing conditions. |
| Adolescent physical health | Parent reports of obesity, diabetes, and asthma at Wave I were used if the adolescent was 18 or younger at the time of interview. We used retrospective reports for adolescents without parent reports available at Wave I, or who were 19 or older at the time of the Wave I interview. Retrospective reports for asthma and obesity were based on responses to the following question at Wave V: “When you were growing up, before age 16, did a doctor, nurse, or other health care provider tell you or your parents/adult caregivers that you have or had any of the following?” We identified retrospective reports of adolescent diabetes from a question on lifetime diagnosis of diabetes administered at Waves IV and V, limiting to those with a self-reported age of diagnosis by age 18. Wave V retrospective reports of diabetes were only used if Wave IV information was unavailable. |
| Midlife indicators of diseases of despair | A sum score of eight indicators of despair across four domains: suicidality, substance misuse, sleep problems, and pain. Each domain contributed two indicators of despair. All indicators were assessed at Wave V. Due to small counts (N with five or more indicators = 10). participants with four or more indicators of despair-related diseases were collapsed into a single category. |
| Suicidality | The two indicators were 1) self-reported suicidal ideation in the past year and 2) self-reported suicide attempt in the past year. Only participants who indicated suicidal ideation in the past year were asked about suicide attempts. |
| Substance misuse | The two indicators were 1) frequent binge drinking and 2) any problematic drug use. Frequent binge drinking included females who reported drinking four or more drinks at a time, and males who reported drinking five or more drinks at a time, three or more times a week in the past 12 months. Any problematic drug use included any reports of prescription drug misuse, any illicit drug use, any opioid misuse, or marijuana use every day or nearly every day in the past 30 days. |
| Sleep problems | The two indicators were 1) trouble falling asleep five or more times a week in the past four weeks and 2) typically sleeping less than five hours a night. Criteria for short sleep duration (< five hours per night) were derived from the Pittsburgh Sleep Quality Index (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). |
| Pain | Pain was characterized by pain medication use. The two indicators were 1) indication of narcotic use in the past four weeks and 2) indication of non-steroidal anti-inflammatory drug (NSAID) use in the past four weeks. Participants responding to web-based interviews self-reported medication use, while medication bottles were referenced for those who received in-home interviews. |
| Midlife indicators of cardiometabolic risk | A sum score of five indicators of cardiometabolic risk included 1) hypertension, 2) diabetes, 3) hyperlipidemia, 4) high-risk waist circumference, and 5) any cardiovascular diagnosis (blood clots, heart disease, heart failure, stroke, or heart attack). All indicators were assessed at Wave V. Due to small counts (N with five indicators = 19), participants with four or five indicators of cardiometabolic risk were collapsed into a single group. |
| Hypertension | In-person high blood pressure reading (level 1 or 2), hypertension medication use in the past four weeks, or self-reported hypertension diagnosis. |
| Diabetes | A fasting glucose > 126 mg/dl, a non-fasting glucose > 200 mg/dl, a HbA1c > 6.5%, self-reported history of non-gestational diabetes, or use of diabetes medication in the past four weeks. |
| Hyperlipidemia | A fasting triglyceride concentration > 500 mg/dl, an LDL-C concentration > 190 mg/dl, self-reported diagnosis of high cholesterol or high triglycerides, or use of antihyperlipidemic medication in the past four weeks. |
| High-risk waist circumference | Guidelines for high-risk waist circumference were from the National Institutes of Health Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults. Participants with a high-risk waist circumference included females with a waist circumference greater than 88 cm and males with a waist circumference greater than 102 cm (“Executive Summary of the Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults,” 1998). |
| Cardiovascular diagnosis | Self-report of physician-diagnosed blood clots, heart disease, heart failure, stroke, or heart attack. |
| **Mediators** |  |
| Low education (primary mediator) | Defined as a high school education or less (Case & Deaton, 2015). Highest education was assessed using the question, “What is the highest level of education that you have achieved to date?” Because this question assessed education received prior to Wave V, we used highest education level at Wave V if available; otherwise, Wave IV information was used. |
| Early-adult substance use (secondary mediator) 1 | Early-adult substance use was measured at Wave IV (ages 24-32) using a sum score of the following indicators: 1) binge drinking 2-3 times per month or more in the past year, 2) marijuana use 2-3 times or more in the past 30 days, 3) any illicit drug use in the past 30 days, and 4) cigarette use 15 days or more in the past 30 days. |
| Early-adult physical inactivity (secondary mediator) 1 | Physical inactivity was assessed at Wave IV using information on participation in moderate and strenuous activities in the past seven days. Consistent with the Center for Disease Control’s guidelines for physical activity in adulthood, participants who engaged in fewer than two strenuous activities, three moderate activities, or three total activities were classified as inactive (Department of Health and Human Services, 2021). The moderate and strenuous activities assessed are in **Supplemental Table 3**. |
| Early-adult fast-food consumption (secondary mediator) 1, 2 | Frequency of fast-food consumption in the past 7 days was assessed at Wave IV using the question, “How many times in the past seven days did you eat food from a fast-food restaurant?” Those who had fast food 7+ times in the past 7 days were combined into a single category. |
| Early-adult healthcare management (secondary mediator) 1, 2 | Healthcare management in the past year was assessed at Wave IV. Questions assessing attendance to routine medical care included “When did you last have a physical exam or routine check-up?” and “In the past 12 months have you had a dental examination by a dentist or dental hygienist?” Three categories were created: 1) those who did not have a routine check-up or dental exam in the past 12 months, 2) those with either, and 3) those with both. |
| **Covariates** |  |
| Age | Age was assessed at Wave V. |
| Male sex | Self-reported sex (male or female) at Wave I. |
| Race | Self-reported race was assessed at Wave I. For participants who reported more than one race, we used the race that they reported “best describes their racial background.” |
| White | Self-reported White race. |
| Black or African-American | Self-reported Black or African-American race. |
| American Indian or Alaska Native | Self-reported American Indian or Alaska Native race. |
| Asian or Pacific Islander | Self-reported Asian or Pacific Islander race. |
| Other | Self-reported race other than those listed above. |
| Hispanic ethnicity | Self-reported ethnicity (Hispanic or non-Hispanic) was assessed at Wave I. |
| Socioeconomic status | Participants’ socioeconomic status was assessed via a social origins score derived from a principal component analysis including parental education, parental occupation, household income, and household receipt of public assistance at Wave I of assessment (Belsky et al., 2018). Overall Add Health Mean = 0, SD = 1. |
| Cognitive ability | Cognitive ability was assessed at Wave I via a modified version of the Peabody Picture Vocabulary Test, which tests receptive vocabulary (Dunn, 1997). Overall Add Health Mean = 100, SD = 15. |

1 Wave IV was used to assess early-adult health behaviors for several reasons. First, we wanted to preserve temporal sequencing to ensure that the mediators did not overlap with our Wave-V outcomes. Second, we chose to assess mediators at Wave IV (ages 24-32 years) over Wave III (18-26 years) because Wave IV more consistently assessed participants during post-collegiate young adulthood, a phase during which health behaviors may be more well-established and consistent.

2 Fast-food consumption and healthcare management were added during the peer-review process.

**Supplemental Table 2. 11-item delinquency scale for conduct disorder**

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| --- | --- | --- | --- |
| **Indicator** | **Question(s)**  **(all start with “In the past 12 months”)** | **Threshold(s) for indicator** | **Other specifications** |
| Deliberate destruction of property | How often did you deliberately damage property that didn’t belong to you? | Any |  |
| Frequent lying | How often did you lie to your parents or guardians about where you had been or whom you were with? | 5 or more times |  |
| Stealing | How often did you steal something worth more than $50? | Any |  |
| Break-in | How often did you go into a house or building to steal something? AND How often did you drive a car without the owner's permission? | Any from either question |  |
| Forced sex | Did you ever physically force someone to have sexual intercourse against her will? | Any | Only classified for males (females were asked a different question) |
| Weapon use | How often did the following happen? You pulled a knife or gun on someone. AND During the past 12 months, how often did the following happen? You shot or stabbed someone. | Any from either question |  |
| Threaten with a weapon | How often did you use or threaten to use a weapon to get something from someone? | Any |  |
| Physically hurt Someone | How often did you hurt someone badly enough to need bandages or care from a doctor or nurse? | Any |  |
| Run away | How often did you run away from home? | 3 or more times |  |
| Skip school | How often did you skip school without an excuse? | 2 or 3 times a month or more | Only available in the Wave I in-school interview |
| Frequent serious fighting | How often did you get into a serious physical fight? | 3 or more times |  |

**Supplemental Table 3. Physical activities in the past 7 days: Distinguishing between moderate and strenuous activities**

|  |  |
| --- | --- |
| **Activities asked about in question** | **Classification of activity level** |
| Bicycle, skateboard, dance, hike, hunt, or do yard work | Moderate |
| Walk for exercise | Moderate |
| Roller blade, roller skate, downhill ski, snow board, play racquet sports, or do aerobics | Moderate |
| Play golf, go fishing or bowling, or play softball or baseball | Moderate |
| Participate in gymnastics, weightlifting, or strength training | Strenuous |
| Participate in strenuous team sports such as football, soccer, basketball, lacrosse, rugby, field hockey, or ice hockey | Strenuous |
| Participate in individual sports such as running, wrestling, swimming, cross-country skiing, cycle racing, or martial arts | Strenuous |

**Supplemental Table 4. Incidence rate ratios (and 95% confidence intervals) for associations of adolescent mental and physical health with midlife diseases of despair, using the full Wave V sample1**

|  |  |
| --- | --- |
| **Predictor** | **Adjusted IRR (95% Confidence Interval)2** |
| Any adolescent psychopathology | 1.57 (1.44, 1.70) |
| Internalizing psychopathology | 1.53 (1.40, 1.67) |
| Externalizing psychopathology | 1.56 (1.39, 1.73) |
| Number of mental-health conditions | 1.41 (1.33, 1.49) |
| Any adolescent physical-health condition | 1.20 (1.07, 1.33) |
| Number of physical-health conditions | 1.19 (1.07, 1.31) |

1 Analytic n=10,342 (all Wave V respondents with information on study variables). The Wave V cross-sectional weight was used in analyses.

2 Adjusted for demographic factors (including age, sex, race, and ethnicity), adolescent socioeconomic status, and adolescent cognitive ability.

**Supplemental Table 5. Incidence rate ratios (and 95% confidence intervals) for associations of prospectively-assessed adolescent mental-health conditions with midlife diseases of despair and cardiometabolic risk**

|  |  |  |  |
| --- | --- | --- | --- |
| **Outcome** | **Predictor1** | **IRR (95% Confidence Interval)** | |
| **Baseline2** | **Adjusted3** |
| Despair-related diseases | Any prospective mental-health condition | 1.55 (1.35, 1.75) | 1.48 (1.28, 1.68) |
| Depression via CES-D | 1.43 (1.25, 1.61) | 1.36 (1.18, 1.54) |
| Conduct disorder | 1.66 (1.37, 1.95) | 1.60 (1.33, 1.87) |
| Cardiometabolic risk | Any prospective mental-health condition | 1.09 (1.00, 1.18) | 1.06 (0.97, 1.14) |
| Depression via CES-D | 1.07 (1.97, 1.16) | 1.04 (0.94, 1.13) |
| Conduct disorder | 1.14 (1.01, 1.26) | 1.11 (0.99, 1.23) |

1 The prospective measure for internalizing psychopathology was depression assessed via the Center for Epidemiological Studies-Depression Scale (CES-D). The prospective measure for externalizing psychopathology was conduct disorder assessed via an 11-item delinquency scale.

2 Baseline models were adjusted for demographic factors including age, sex, race, and ethnicity.

3 Adjusted models were also adjusted for adolescent socioeconomic status and adolescent cognitive ability.

**Supplemental Table 6. Incidence rate ratios (and 95% confidence intervals) for associations of adolescent physical-health problems with midlife diseases of despair and cardiometabolic risk**

|  |  |  |
| --- | --- | --- |
|  | **IRR (95% CI)** | |
| **Baseline1** | **Adjusted2** |
| Diseases of despair | 1.18 (1.01-1.36) | 1.16 (0.98-1.33) |
| Cardiometabolic risk | 1.49 (1.38-1.60) | 1.47 (1.36-1.59) |

1Baseline models were adjusted for demographic factors including age, sex, race, and ethnicity.

2Adjusted models were also adjusted for adolescent socioeconomic status and adolescent cognitive ability.

**Supplemental Table 7.** **Testing mediation of the association of adolescent psychopathology with midlife indicators of diseases of despair**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Mediator** | **Total effect** | **Direct effect** | **Total**  **indirect effect** | **% mediation1** |
| Low education | 1.67 (1.48-1.87) | 1.64 (1.46-1.84) | 1.01 (1.002-1.03) | 2.1 |
| Early-adult substance use – including substance use indicators in outcome | 1.65 (1.47-1.84) | 1.44 (1.29-1.60) | 1.14 (1.10-1.18) | 21.5 |
| Early-adult substance use – excluding substance use indicators from outcome | 1.78 (1.52-2.06) | 1.65 (1.42-1.90) | 1.08 (1.04-1.12) | 10.3 |
| Early-adult physical inactivity2 | 1.67 (1.49-1.87) | 1.67 (1.49-1.87) | 1.00 (0.99-1.00) | -- |
| Early-adult fast-food consumption | 1.67 (1.49, 1.87) | 1.66 (1.49, 1.86) | 1.00 (0.99, 1.02) | -- |
| Early-adult healthcare management | 1.67 (1.49, 1.87) | 1.65 (1.47, 1.84) | 1.02 (0.999, 1.03) | -- |

All models adjust for demographic factors including age, sex, race, ethnicity, socioeconomic status, and cognitive ability. Bootstrap confidence intervals with 500 iterations were used to estimate 95% confidence intervals.

1 Percent mediation is only presented for tests of mediation with statistically-significant indirect effects and was calculated before estimates were rounded to the nearest hundredth. Direct and indirect effects do not always sum exactly to the total effect due to rounding.

2 Findings were consistent across two additional measures of physical inactivity: 1) sum of total number of instances of moderate or strenuous activity in the past 7 days, and 2) sum of total number of instances of strenuous activity in the past 7 days.

**Supplemental Table 8. Testing mediation of the association of adolescent psychopathology with midlife indicators of cardiometabolic risk**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Mediator** | **Total effect** | **Direct effect** | **Total**  **indirect effect** | **% mediation1** |
| Low education | 1.13 (1.04-1.21) | 1.12 (1.03-1.20) | 1.01 (1.00-1.02) | -- |
| Early-adult substance use | 1.12 (1.04-1.21) | 1.13 (1.05-1.22) | 0.99 (0.98-1.01) | -- |
| Early-adult physical inactivity2 | 1.13 (1.04-1.22) | 1.13 (1.05-1.22) | 1.00 (0.99-1.00) | -- |
| Early-adult fast-food consumption | 1.12 (1.04, 1.22) | 1.12 (1.04, 1.22) | 1.00 (0.99, 1.01) | -- |
| Early-adult healthcare management | 1.13 (1.04, 1.22) | 1.13 (1.04, 1.22) | 1.00 (0.99, 1.01) | -- |

All models adjust for demographic factors including age, sex, race, ethnicity, socioeconomic status, and cognitive ability. Bootstrap confidence intervals with 500 iterations were used to estimate 95% confidence intervals.

1 Percent mediation is not presented as indirect effects were not statistically significant.

2 Findings were consistent across two additional measures of physical inactivity: 1) sum of total number of instances of moderate or strenuous activity in the past 7 days, and 2) sum of total number of instances of strenuous activity in the past 7 days.

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