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Developmental Timing of Suicide Attempts and Cardiovascular Risk During Young Adulthood

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Objective: Self-control/self-regulation has received increased attention in health research. Suicide attempts index severe dysregulation in emotional, behavioral, and/or physiological domains. The current study tested whether own and/or others' suicide attempts during the early life course predicted cardiovascular risk by young adulthood and whether developmental timing of suicide attempts, sex of the person, and source of suicide attempts exposure modified these associations. ***Method:*** Data came from the National Longitudinal Study of Adolescent to Adult Health (Add Health). At each assessment during Waves I–IV (covering approximately ages 12–32 years), participants reported whether they and/or a friend/family member had attempted suicide. At Wave IV, trained interviewers assessed participants' obesity and hypertension and collected bloodspots from which high-sensitivity C-reactive protein (hs-CRP) was assayed. Sample sizes in the present analyses ranged from $n = 7{,}884$ to $n = 8{,}474$. ***Results:*** Exposure to own and others' suicide attempts during adolescence was relatively common. In males, suicide attempts during adolescence (~age 15 years) were associated with hypertension and elevated inflammation more than 1 decade later. Associations among suicide attempts by others and cardiovascular risk also emerged. ***Conclusions:*** Exposure to one's own or others' severe dysregulation in the form of suicide attempts during the early life course signals risk for cardiovascular health problems by the late twenties. Adolescent males who attempted suicide and individuals exposed to suicide attempts in their social network may benefit from a dual focus on mental and physical health in care.

Keywords: Add Health, cardiovascular risk, inflammation, sex differences, suicide attempt

Supplemental materials: http://dx.doi.org/10.1037/hea0000373.supp

Suicide attempts were on the rise in the recent decade of economic downturn in the United States (e.g., Reeves et al., 2012). Indeed, many adolescents and young adults attempt suicide or are exposed to suicide attempts of others (e.g., Kessler, Borges, & Walters, 1999; Nock et al., 2013). Understandably, a priority has been to identify and prevent precursors of suicide attempts among young people (e.g., Fergusson, Beautrais, & Horwood, 2003; Lewinsohn, Rohde, & Seeley, 1994). Less is currently known about outcomes of early life course suicide attempts, although long-term impairments in psychosocial, psychiatric, educational, financial, and legal domains have been documented (e.g., Brière, Rohde, Seeley, Klein, & Lewinsohn, 2015; Fergusson, Horwood, Ridder, & Beautrais, 2005).

Physical health is rarely examined in follow-up studies of suicide attempts. However, suicide attempts index severe dysregulation in emotional, behavioral, and physiological domains; such dysregulation has been linked to poor physical health years later (e.g., Appleton, Loucks, Buka, Rimm, & Kubzansky, 2013; Copeland, Shanahan, Worthman, Angold, & Costello, 2012; Melhem et al., 2015; Moffitt et al., 2011). Suicide attempts also mark exposure to stigma, social isolation, unhealthy behaviors, and lower educational/professional attainment after the attempt (e.g., Mars et al., 2014); these factors have also each been linked with poor health.

Initial evidence for suicide attempt-cardiovascular risk associations came from New Zealand's Dunedin birth cohort, in which individuals who attempted suicide before 24 years of age were more likely to have elevated inflammation and Framingham heart risk scores and to meet criteria for metabolic syndrome by their late thirties (Goldman-Mellor et al., 2014). After this pioneering work, several important nuances in suicide attempt-cardiovascular

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risk associations remain to be understood, including the roles of developmental timing of suicide attempt, sex of the person, and source of suicide attempt exposure (e.g., own vs. others' attempt). The present prospective-longitudinal study uses data from the U.S. National Longitudinal Study of Adolescent to Young Adult Health (Add Health) to examine adolescent and young adult suicide attempt exposures in the prediction of three cardiovascular risk indicators—obesity, hypertension, and elevated C-reactive protein—when participants were in their late twenties.

Nuances in Suicide Attempt-Cardiovascular Risk Associations

Two hypotheses regarding the developmental timing of suicide attempts are possible. Earlier attempts could index more severe (a) etiologies such as psychosocial adversity and biobehavioral dysregulation, (b) manifestations of associated mental health conditions (e.g., depression), and (c) consequences compared to later suicide attempts. Accordingly, an early-onset hypothesis suggests that being exposed to suicide attempts earlier (e.g., during adolescence) as compared to later (e.g., during young adulthood) will be associated with greater cardiovascular risk. Support for this hypothesis comes from research establishing more severe and pervasive long-term consequences of earlier- as opposed to later-onset depressions (e.g., Kaufman, Martin, King, & Charney, 2001; Weissman et al., 1999). Alternatively, a recency hypothesis suggests that more recent experiences of suicide attempts will be most consequential for health. Support for this hypothesis comes from work suggesting that the adverse consequences of stressors and life events are often time-limited, lasting no longer than a couple of months (e.g., Brown & Harris, 1978; Kessler, Davis, & Kendler, 1997). Accordingly, cardiovascular risk could be greater among young adults exposed to suicide attempts recently versus during adolescence.

A person's sex could also modify suicide attempt-cardiovascular risk associations, especially for adolescent suicide attempters. Suicide attempts are twice as common among adolescent females than males (e.g., Lewinsohn, Rohde, Seeley, & Baldwin, 2001). The etiology of adolescent suicide attempts could be sex differentiated. In females, social contagion and temporarily heightened sensitivity to interpersonal stressors likely play a greater role in suicide attempts during adolescence (e.g., Abrutyn & Mueller, 2014; Hawton, Saunders, & O'Connor, 2012; Natsuaki et al., 2009). The effects of these precipitators may be time-limited, without long-term consequences for cardiovascular health. In contrast, suicide attempts by adolescent males (and females during other periods of their lives) may be precipitated by more severe and chronic risk dynamics, including exposure to severe psychosocial adversity and/or biobehavioral dysregulation (e.g., Brent, Baugher, Bridge, Chen, & Chiappetta, 1999), which, in turn, could contribute to long-term physical health risks associated with suicide attempts. Consequently, adolescent suicide attempt-cardiovascular risk associations could be stronger in adolescent males than females. Similar sex differences may not be found when studying suicide attempts (and cardiovascular risk) at other ages (e.g., Goldman-Mellor et al., 2014).

Finally, the source of suicide attempt exposure could modify associations with cardiovascular risk. Young people can experience their own suicide attempt. However, even more commonly, they are exposed to others' (e.g., friends', family members') suicide attempts (e.g., Bearman & Moody, 2004; Resnick et al., 1997). Network suicide attempts constitute a severe life event and interpersonal stressor (e.g., Kendler & Karkowski-Shuman, 1997) that could precipitate a chain of stress-related physiological responses and unhealthy behaviors, which could contribute to increases in cardiovascular risk (Abrutyn & Mueller, 2014). Network suicide attempts also mark exposure to another person's severe dysregulation, with possible risks for "transmission"/contagion (e.g., Borowsky, Ireland, & Resnick, 2001). The literature on network life events suggests that undesirable life events occurring to others in one's social network impact females' mental health more negatively than males' (e.g., Kendler & Karkowski-Shuman, 1997). Accordingly, network suicide attempts could have more severe physical health consequences for females than males.

Method

Participants

Data came from Add Health, a U.S. nationally representative sample of adolescents who were first interviewed in grades 7–12. The sampling frame for Add Health included all high schools in the United States, from which $N = 80$ were randomly selected to participate in the survey with an additional 52 feeder middle schools. Approximately 200 students from each school were randomly selected for in-home interviews ($N = 20{,}745$), which were conducted at Wave I (1994–95; $M = 14.95$ years; range: 12–19), Wave II (1996; $M = 15.86$ years; range: 13–20), Wave III (2001–2002; $M = 21.31$ years; range: 18–26), and Wave IV (2007–2008; $M = 27.81$ years; range: 24–32). Add Health participants provided written informed consent for participation in all aspects of Add Health in accordance with the University of North Carolina School of Public Health Institutional Review Board guidelines.

For the present paper we examined $n = 8{,}387$ for obesity, $n = 8{,}474$ for hypertension, and $n = 7{,}884$ for high-sensitivity C-reactive protein (hs-CRP). On the basis of the intake sample size of $N = 20{,}745$ at Wave I, 24% did not participate in in-home interviews at Wave IV (which took place ~13–14 years after Wave I). Four percent of participants had missing sampling weights. For the present analyses, we also excluded participants with missing data at Waves II and III because their data were not informative regarding our research questions about the role of the developmental timing of suicide attempts in predicting later cardiovascular risk. Thirteen percent of the intake sample had missing data at Wave II that were missing because of the study design. Specifically, according to the Add Health sample design, Wave I respondents who were in 12th grade or in the disability sample were not eligible to be reinterviewed at Wave II. An additional 5% and 8% were eligible to participate in Waves II and III, respectively, but did not. Finally, approximately 4–5% of the intake sample had missing data on the Wave IV obesity and hypertension outcomes and 7% on the Wave IV hs-CRP outcome.

There were some significant differences between the starting sample and the analytic sample, most of which were due to the exclusion of older adolescents at Wave II by study design. Specifically, participants who were older (15.9 vs. 14.9 years, $p < .001$), had slightly higher body mass index (BMI; 22.6 vs. 22.2 kg/m^2, $p < .001$), and reported slightly more depressive symptoms (5.8 vs. 5.6, $p < .001$) at Wave I were more likely to be excluded from our analytic sample. Differences in BMI and depressive

symptoms were accounted for by age ($p = .565$ and $p = .663$ for these differences when age was included). In addition, the analytic sample was slightly more likely to be female and White ($p < .001$, respectively), which was primarily due to patterns of participation in Wave IV biomarker assessments. As described earlier, the two main reasons for missing data in the current analyses were missingness on the outcome variables and missingness by study design. Given that the use of multiple imputation methods is unsuitable for these reasons of missingness, such methods were not used here. This approach is consistent with other work using all four waves of Add Health data (e.g., Hatzenbuehler, Slopen, & McLaughlin, 2014). The inclusion of variables on which the initial versus the analytic sample differed did not change the overall patterns of results.

Assessment of Young Adult Cardiovascular Risk

Field interviewers measured respondent height, weight, and systolic and diastolic blood pressure at Wave IV. Blood samples were obtained as described in the Add Health documentation (Whitsel et al., 2013). Dried blood spots were assayed at the University of Washington Medical Center Immunology Laboratory. Documentation of the Add Health hs-CRP assay and quality control are available online (Whitsel et al., 2013). In brief, a sandwich enzyme-linked immunoabsorbent assay (ELISA) method was adapted from a previously published method (McDade, Burhop, & Dohnal, 2004). Values from blood spots and paired plasma samples were highly correlated ($r = .98$) in a cross-validation study. Intraassay variation was 8.1% and interassay variation was 11%.

Obesity, hypertension, and inflammation were each assessed on different scales. To increase comparability across outcomes, we used clinically meaningful categories. Obesity was coded as (a) <25 kg/m^2 = *normal*, (b) 25–29 kg/m^2 = *overweight*, (c) 30–34 kg/m^2 = *moderately obese*, and (d) ≥ 35 kg/m^2 = *severely obese* (National Institutes of Health & National Heart Lung & Blood Institute, 1998). Pregnant women ($n = 312$; 6.5% of females) were omitted from obesity analyses. Hypertension was coded as (a) systolic <120 mmHg and diastolic <80 mmHg = *normal*, (b) systolic 120–139 mmHg or diastolic 80–89 mmHg = *prehypertension*, and (c) systolic $\geq 140 +$ mmHg or diastolic ≥ 90 mmHg or taking antihypertensive medications or ever diagnosed as hypertensive by a physician = *hypertension* (Chobanian et al., 2003). C-reactive protein was coded as (a) <1.0 mg/L = *low risk*, (b) 1.0–3.0 mg/L = *moderate risk*, (c) >3.0–10.0 mg/L = *high risk*, and (d) >10.0 mg/L = *very high risk* (Pearson et al., 2003). Glycosylated hemoglobin and lipids are available in the dataset but were not examined here because of their lower reliability in nonfasting individuals.

Assessment of Suicide Attempts

Individual suicide attempts were assessed during in-home interviews at all four waves using self-administered audio computer-assisted interviewing and a 12-month timeframe. Among adolescents, such computer-assisted interviews have been shown to have greater reliability for sensitive questions compared with interviewer-based interviews (e.g., Turner et al., 1998). Respondents were asked "Did you ever seriously think about committing suicide?" and "How many times did you actually attempt suicide?" Based on the latter item, suicide attempts were coded as a binary indicator. Network suicide attempts during the past 12 months were measured by asking "Have any of your family members tried to kill themselves?" and "Have any of your friends tried to kill themselves?" in Waves I–III. In Wave IV, these questions were combined. Our analyses focus on combined friends' and family members' suicide attempts.

Developmental timing of suicide attempt was coded based on participants' age at the time of interview. Age 18 served as the cutpoint for distinguishing between adolescence and young adulthood because it approximately marks the end of the high school years in the United States and a decline in rates of suicide attempts (Lewinsohn et al., 2001). Using individual suicide attempts as an example, developmental timing was coded as 1 = *no attempt*, 2 = *adolescent attempt* (i.e., ≥ 1 suicide attempt at ≤ 18 years), and 3 = *young adult attempt* (i.e., ≥ 1 attempt at ≥ 19 years). Participants who reported both adolescent and young adult suicide attempts were included in the adolescent attempt category because their number was insufficient for conducting separate analyses. Results remained unchanged when this group was excluded.

Assessment of Covariates

Several covariates are associated with suicide attempts, cardiovascular health, or both and were incorporated in fully adjusted models. Demographic characteristics included a continuous measure of age at Wave I (in years), sex (1 = *female*), and race/ethnicity (1 = *White*, 2 = *Black*, 3 = *non-White Hispanic*, 4 = *other*, with 1 serving as the reference category). Measures of socioeconomic status included parent-reported parental education at Wave I, with 1 = *high school or less*, 2 = *some college*, and 3 = *college or more*. Maximum parental education was used in two-parent households. Self-reported young adult respondent education at Wave IV used the same coding scheme as parental education.

Psychological covariates. Depressive symptoms (all waves) were measured using an abbreviated nine-item Center for Epidemiologic Studies Depression Scale (CES-D). Items included whether the respondent "could not shake off the blues" or "felt sad" over the past 30 days. Responses ranged from 1 = *never or rarely* to 3 = *most of the time or all of the time*. Participants' depressive symptoms were averaged across waves. At Wave IV, participants also reported whether a health-care provider had ever told them that they had depression, posttraumatic stress disorder, or any other anxiety disorder (1 = *diagnosis*).

Health behaviors (Wave IV) included a binary measure of cigarette smoking (1 = *current smoker*), frequency of alcohol consumption over the past 12 months (0 = *none* to 6 = *every day or almost every day*), and frequency of physical activity (total number of times of sports participation per week, capturing light to strenuous physical activities). Final models for females adjusted for binary variables indicating self-reported pregnancy and hormonal contraceptives use (1 = *pregnant*, 1 = *hormonal contraceptives use*, respectively).

Several additional covariates of hs-CRP specifically were also assessed (Wave IV) and used only in the hs-CRP analyses. Participants were asked whether a doctor, nurse, or other health-care provider had ever told them that they had diabetes or respiratory disease (1 = *diagnosis*). The subclinical symptoms scale counted

whether participants reported having had a fever, night sweats, nausea or vomiting or diarrhea, blood in stool or urine, frequent urination, and skin rash or abscess in the past 2 weeks (0 = *0 symptoms*, 1 = *1 symptom*, 2 = *2 symptoms*, 3 = *≥3 symptoms*). The infectious/inflammatory diseases scale counted lifetime diagnosis of asthma or chronic bronchitis or emphysema; lifetime diagnosis of hepatitis C; and gum disease, active infection, injury, acute illness, surgery, and active seasonal allergies in the past 4 weeks (0 = *0 diseases*, 1 = *1 disease*, 2 = *2 diseases*, 3 = *≥3 diseases*). Medication use indicated whether respondents were taking (a) nonsteroidal anti-inflammatory/salicylate medication, including in the past 24 hr; (b) cox-2 inhibitor; (c) inhaled corticosteroid; (d) corticotropin/glucocorticoid; (e) antirheumatic/antipsoriatic; or (f) immunosuppressive medications in the past 4 weeks (see also Add Health documentation; Whitsel et al., 2013).

Finally, adolescent observations counted the number of adolescent observations for each respondent, which differed somewhat across respondents, because we used age (not wave of assessment) for defining adolescence/young adulthood.

Variables used in follow-up analyses. Suicidal ideation in the past 12 months was measured at each wave using a single item: "Did you ever seriously think about committing suicide?" Suicidal injury in the past 12 months was measured by asking "Did any attempt result in an injury, poisoning, or overdose that had to be treated by a doctor or nurse?" Self-reported BMI was available during Wave I of Add Health—when interviewer-measured BMI was not available. To gauge the reliability of this indicator, we correlated Wave IV self-reported and interviewer-measured BMI. The two measures were highly correlated at $r = .94$, $p < .001$. Thus, Wave I self-reported BMI is likely a highly reliable indicator of BMI. Additional covariates that were used in follow-up analyses (e.g., markers of early adversity and impulsivity) are described in Supplement 1 online.

Analytic Strategy

Associations among developmental timing of individual and network suicide attempts and cardiovascular risk were tested using ordinal logistic regression models for each outcome, separately for females and males, and separately for each attempt source. Table 3 summarizes results from fully covariate-adjusted models that simultaneously entered all covariates. All analyses were performed using no suicide attempt as the reference category. In follow-up analyses, we recoded the developmental timing variable to contrast adolescent versus young adult timing. We also analyzed the entire sample to test sex differences. Significant developmental timing and sex differences are reported in the text and explained in Table 3. All analyses were conducted using Stata 13. Survey weights were used to account for unequal chances of selection. Error variances were adjusted for the clustered sampling design. The discussion prioritizes results from fully adjusted models and patterns of significant results.

Results

Descriptive Statistics

Table 1 shows that individual suicide attempts were more common in adolescence than in young adulthood and among females than males. Network suicide attempts were notably more common than individual suicide attempts. Adolescent network suicide attempts were more commonly reported by females than by males. Approximately two in five female adolescents reported a network suicide attempt, compared with approximately one in five male adolescents. Network and individual suicide attempts were associated during adolescence and young adulthood (odds ratio [*OR*] = 4.82, confidence interval [CI]: 3.63–6.40 and *OR* = 2.17, CI: 1.45–3.27, respectively). Sex differences in the prevalence of network suicide attempts decreased significantly from adolescence to young adulthood.

Table 2 shows descriptive statistics for young adult cardiovascular risk indicators. Consistent with work on recent cohorts (Reither, Olshansky, & Yang, 2011), only the minority of young adults fell into the normal or low-risk ranges. Males were at higher risk for overweight/obesity and pre-/hypertension compared with females. Females were at higher risk for elevated inflammation compared with males (see also, Shanahan, Freeman, & Bauldry, 2014). Descriptive statistics of all covariates used in the fully adjusted models can be found in Supplement 2 online.

Predictive Analyses

The left half of Table 3 shows results from analyses using individual adolescent and young adult suicide attempts to predict young adult cardiovascular risk (obesity, hypertension, elevated hs-CRP) in separate covariate adjusted models for males and for females. The right half of Table 3 shows results from parallel analyses using network adolescent and young adult suicide attempts as predictors. Note that the table in Supplement 3 online shows that results were similar when individual and network suicide attempts were simultaneously entered into the models. The table in Supplement 4 online also shows corresponding results from bivariate analyses.

Individual suicide attempts had no significant associations with obesity. However, individual suicide attempts during adolescence were associated with both young adult hypertension and elevated hs-CRP in males, but not in females. For example, in the fully adjusted models, males who had attempted suicide during adolescence had 70% greater odds of being in the next higher young adult hypertension category compared with males who had not attempted suicide during adolescence. These analyses adjusted for young adult BMI. Follow-up analyses using the entire sample confirmed significant adolescent suicide attempt by sex interactions for both hypertension and hs-CRP (*OR* = 0.56, CI: 0.34–0.93, $p = .024$, and *OR* = 0.55, CI: 0.35–0.89, $p = .013$, respectively).

Network suicide attempts were associated with obesity in females, regardless of timing of attempt. Adolescent, but not young adult network attempts, were associated with obesity in males. Follow-up analyses using the entire sample revealed a marginally significant young adult network attempt by sex interaction for obesity (*OR* = 1.39, CI: 0.96–2.02, $p = .081$). Network suicide attempts during young adulthood were also associated with hypertension in females, but not in males (*OR* = 0.80, CI: 0.60–1.05, $p = .099$ for the adolescent-young adult contrast). Finally, network suicide attempts during young adulthood were associated with elevated hs-CRP in males. Using the entire sample, a young adult network suicide attempt by sex interaction emerged in the prediction of hs-CRP with adolescent network attempt as the reference category (*OR* = 1.71, CI: 1.13–2.59, $p = .010$). Thus, young adult network suicide attempts (relative to adolescent network attempts) were more predictive of hs-CRP in males than in females.

Table 1
Weighted Prevalence of Adolescent and Young Adult Individual and Network Suicide Attempts

Source and timing of suicide attempt	Full sample (N = 8,474)	Males (n = 3,815)	Females (n = 4,659)	Sex difference p	Age difference p	Sex by age difference p
Individual suicide attempt						
None	91.1	94.4	87.9	<.001	<.001	.080
Adolescent	6.4	3.6	9.1			
Young adult	2.5	2.0	3.0			
Network suicide attempt						
None	59.2	66.7	52.2	<.001	<.001	<.001
Adolescent	30.9	22.6	38.7			
Young adult	9.9	10.7	9.1			

Follow-Up Analyses

A first set of follow-up analyses tested whether cardiovascular risk in young adult males became greater with increasing "severity of suicidality" during adolescence. Data on method of attempt were not collected in Add Health, but proxies of severity were available (ideation, attempt, injury from attempt). Results for hypertension revealed that the size of the *OR*s increased from ideation (OR = 1.37) to attempt (OR = 1.71). For hs-CRP, *OR*s increased from ideation (OR = 1.27) to attempt (OR = 1.64) to injury (OR = 2.45). Figure 1 illustrates how hs-CRP risk increased along the suicidality severity gradient for males. When we created a continuous adolescent suicidality severity index (coded 0 = *no suicidal ideation or attempt*, 1 = *suicidal ideation*, 2 = *suicide attempt*, 3 = *injury from suicide attempt*), the continuous index predicted adult hs-CRP categories (OR = 1.19, CI: 1.01–1.40). These analyses lend support for a graded association between suicidal cognitions/behaviors and severity of later inflammation. Nevertheless, such gradients should be interpreted with caution given that suicidal cognitions and behaviors are heterogeneous and transitions from ideation to attempt to injury do not necessarily reflect a continuous process.

A second set of follow-up analyses probed the robustness of major findings. First, considering that suicide attempts during adolescence often co-occur with psychosocial adversity, we controlled for single parenthood and childhood maltreatment. Second, because adolescent suicide attempts could be an indicator of impulsivity, we controlled for available indicators of impulsivity (e.g., cigarette, alcohol, and marijuana use; early sexual debut; violent and nonviolent delinquency). Third, all analyses predicting hypertension and hs-CRP were repeated without pregnant women. Fourth, all hs-CRP analyses were repeated excluding (a) women using hormonal contraceptives and (b) individuals with two or more subclinical illness symptoms. Fifth, all analyses were repeated combining the "high risk" and "very high risk" hs-CRP groups into one category. Finally, obesity analyses were repeated controlling for Wave I obesity. In these robustness checks, the overall pattern of findings remained similar (detailed description of robustness-check covariates available in Supplement 1 online).

Discussion

Exposure to severe dysregulation in the form of one's own or close others' suicide attempts during the early life course is common. Almost 10% of young people in our analytic sample reported suicide attempts between the high school and young adulthood years; more than 40% reported being aware of a family member's or friend's suicide attempt. Exposure to suicide attempts could signal risk for the premature development of cardiovascular risk (Goldman-Mellor et al., 2014). We drew on the prospective Add

Table 2
Weighted Percentage for Young Adult Cardiovascular Risk Categories in Analytic Sample

Cardiovascular risk indicator	Full sample	Males	Females	p for sex difference
Obesity (N = 8,387)				
Normal (<25.0)	35.1	31.1	39.1	<.001
Overweight (25.0–29.9)	28.6	33.0	24.1	
Obese (30.0–34.9)	18.0	20.1	15.9	
Severely obese (≥35.0)	18.3	15.8	20.9	
Hypertension (N = 8,474)				
Normal (systolic <120 and diastolic <80 mmHg)	32.1	16.5	46.7	<.001
Prehypertension (systolic 120–139 or diastolic 80–89 mmHg)	43.3	50.4	36.6	
Hypertension (systolic ≥140 or diastolic ≥90 or ever diagnosed hypertensive or on antihypertensive medication)	24.6	33.1	16.7	
C-reactive protein (N = 7,884)				
Normal/low risk (<1.0)	32.3	39.6	25.7	<.001
Moderate risk (1.0–3.0)	27.4	30.4	24.8	
High risk (>3.0–10.0)	27.8	23.8	31.4	
Very high risk (>10.0)	12.5	6.2	18.1	

Table 3
Adjusted Associations Among Individual and Network Suicide Attempts and Cardiovascular Outcomes in Males and Females

Sex and developmental timing	Individual Suicide Attempt		Network Suicide Attempt	
	Obesity		Obesity	
Males				
Adolescence	1.07 (0.56–2.05)		**1.25*** (1.03–1.53)	Adult network suicide attempt by sex interaction: $p = .081$
Adulthood	0.59† (0.35–1.00)		1.19 (0.90–1.57)	
Females				
Adolescence	0.90 (0.66–1.23)		**1.32**** (1.12–1.56)	
Adulthood	1.42 (0.77–2.60)		**1.47**** (1.11–1.95)	
	Hypertension		Hypertension	
Males				
Adolescence	**1.70*** (1.01–2.84)	Adolescent individual suicide attempt by sex interaction: $p = .024$	0.96 (0.78–1.18)	Developmental timing of network suicide attempt interaction in females: $p = .099$
Adulthood	0.62 (0.23–1.68)		1.13 (0.84–1.51)	
Females				
Adolescence	0.95 (0.75–1.20)		1.11 (0.92–1.33)	
Adulthood	0.97 (0.50–1.91)		**1.39*** (1.06–1.83)	
	hs-CRP		hs-CRP	
Males				
Adolescence	**1.66*** (1.08–2.54)	Adolescent individual suicide attempt by sex interaction: $p = .013$	0.94 (0.77–1.16)	Developmental timing of network suicide attempt × Sex interaction: $p = .010$
Adulthood	1.09 (0.59–2.00)		**1.37*** (1.02–1.84)	
Females				
Adolescence	0.94 (0.71–1.25)		0.99 (0.83–1.18)	
Adulthood	0.87 (0.58–1.32)		0.81 (0.62–1.06)	

Note. *OR*s and 95% CIs (in parentheses). Within the six cells of results, the *OR*s highlighted in grey are those that were different from one another. Adjusted models included the following covariates: race/ethnicity (Black, Hispanic, other), age at Wave I, parental education, respondent education, psychological symptoms/diagnoses (depressive symptoms, lifetime diagnosis of depression, lifetime diagnosis of PTSD/anxiety disorder), health behaviors (current cigarette smoker, frequency of alcohol consumption, frequency of physical activity), number of adolescent observations, obesity, and physical illness and medications (lifetime diagnosis of diabetes, respiratory disease, subclinical symptoms, recent infections, antiinflammatory medication use, hormonal contraceptive use, and current pregnancy). Pregnant women were omitted from the obesity models.
$^{\dagger}p < .10$. $^{*}p < .05$. $^{**}p < .01$. **Bolded** odds ratios are significant at $p < .05$.

Health study and revealed that individual suicide attempts during adolescence (~15 years of age) were associated with hypertension and elevated inflammation in males more than 1 decade later (~27 years of age). Network suicide attempts were also associated with later cardiovascular risk, but with less clear-cut effects of sex and developmental timing on these associations. Taken together, associations among suicide attempts and cardiovascular risk were contingent on developmental timing, sex of the person, source of exposure, and specific indicator of cardiovascular risk.

For individual suicide attempts, the early-onset hypothesis was supported in males for hypertension and hs-CRP. Adolescent suicide attempts among males could mark severe psychosocial adversity (Briére et al., 2015) and/or dysregulation of emotions (e.g., depression), behaviors (e.g., impulsivity), and physiology (e.g., hypothalamic-pituitary-adrenal axis dysregulation). They could also result in stigma, social isolation, unhealthy behaviors, and lower educational and job accomplishments (e.g., Mars et al., 2014).

Our findings remained significant when controlling for several markers of adversity and for potential select consequences of suicide attempts (e.g., reduced educational attainment). They also remained significant when controlling for indicators of emotional

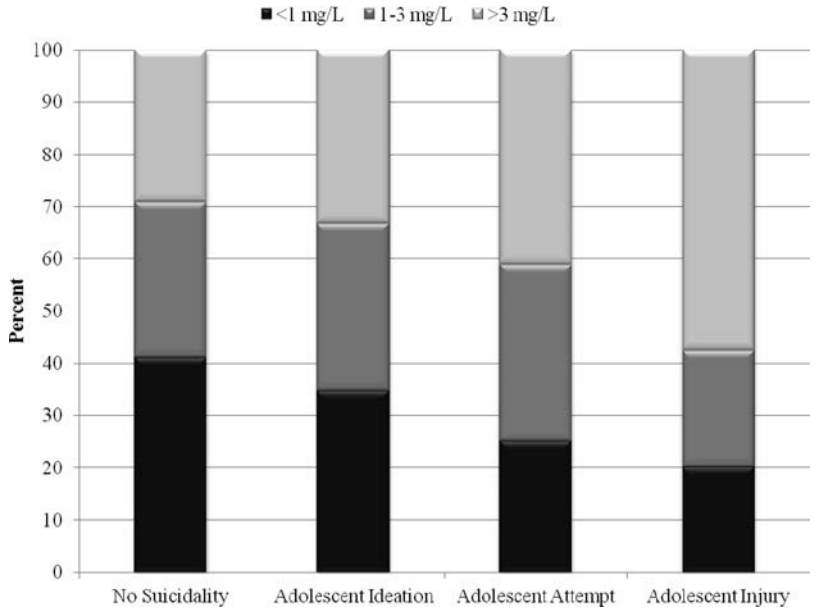


Figure 1. Percentage of males in clinical reference ranges of C-reactive protein by severity of suicidal behavior ($N = 3{,}442$).

and behavioral dysregulation, although these indicators likely only imperfectly captured these constructs given the large-scale, field-based study design. Indeed, although our study further illuminated the signal function of adolescent individual suicide attempts for future cardiovascular risk (Goldman-Mellor et al., 2014), smaller, laboratory-based studies are needed to illuminate how suicide attempts signal risk for cardiovascular risk a decade later and the potential role played by different domains of dysregulation. Such laboratory-based studies could also include observational and physiological measurements of dysregulation and stress responses that may have downstream consequences for cardiovascular risk.

Individual suicide attempts were not associated with cardiovascular risk among females. Suicidal behaviors are relatively common among adolescent females (Lewinsohn et al., 2001), and a sex-differentiated etiology of adolescent suicide attempts could play a role in sex-differentiated associations with cardiovascular risk. For example, social contagion and temporarily heightened sensitivity to interpersonal stressors likely play a greater role in adolescent females' than males' suicide attempts (e.g., Abrutyn & Mueller, 2014; Hawton et al., 2012; Natsuaki et al., 2009). The effects of these precipitators may be time-limited, without long-term consequences for cardiovascular health. There may also be sex differences in help-seeking behaviors, treatment access and response, success at restoring regulation and healthy behaviors, and coping with stigma after adolescent suicide attempts (e.g., Calear, Batterham, & Christensen, 2014; Rhodes et al., 2013).

Associations between individual suicide attempts during young adulthood and cardiovascular risk did not emerge. This was surprising given temporal proximity of measurements and other findings from cross-sectional work with clinical samples indicating that adult suicide attempters had elevated inflammation (e.g., Janelidze, Mattei, Westrin, Träskman-Bendz, & Brundin, 2011). Sleeper/incubation effects from suicide attempts to later health risks are possible, meaning that it could take some time for the precursors and consequences of young adult suicide attempts to manifest themselves in health. For example, young adult suicide attempts could be precipitated by adversities such as recent job loss (Dalglish, Melchior, Younes, & Surkan, 2015; Gassman-Pines, Ananat, & Gibson-Davis, 2014) or divorce; the consequences of these adversities could take months or years to manifest themselves in measurable decreases in health. Cardiovascular risk after suicide attempts in young adulthood may also be heightened only in select cases (e.g., in treatment-seeking cases that may present with more impairing and severe mental health problems compared with individuals who do not seek treatment).

Network suicide attempts were also associated with later cardiovascular risk, but sex and developmental timing effects were less clear-cut. Network attempts appeared to have the most robust associations with obesity and hypertension in young adult females, although statistical tests of sex differences were not always significant. A female preponderance of network attempt-cardiovascular risk associations would be consistent with prior research reporting that females tend to be more affected by events in their social networks than males (e.g., Bearman & Moody, 2004; Kendler & Karkowski-Shuman, 1997). Future research should test whether our findings of sex differences hold in different samples.

Network attempts could precipitate a chain of unhealthy behaviors, cognitions, and changes in social support structures that could contribute to increases in cardiovascular risk (Abrutyn & Mueller, 2014). It is also possible that severe dysregulation in the form of suicide attempts can, to some extent, be "transmitted" in social networks, which could result in increased physical health risk in the network of a person who attempted suicide. Future research should examine how long into the future predictions from network suicide attempts hold and the roles of relationship to the person who attempted suicide and psychological distress after exposure to a network suicide attempt. Of note, social networks during the

young adult years are likely smaller and more tight-knit compared with the networks of the adolescent years. Thus, future work should aim at disentangling potential confounding between timing of network suicide attempt and size and quality of the network. Future research should also continue to test whether associations between network suicide attempts and obesity and hypertension are stronger in females than in males.

Of note, each sex had one cardiovascular risk outcome that had no consistent pattern of associations with suicide attempts: obesity in males and hs-CRP in females. Obesity is a BMI-based measure. Males' BMI during young adulthood could be elevated due to adipose tissue or lean muscle mass. Likewise, hs-CRP in females could be elevated due to stress and unhealthy behaviors or due to the hormonal and metabolic changes of the reproductive years (e.g., Shanahan et al., 2014; Stuebe & Rich-Edwards, 2009). Given the heterogeneity of reasons for high BMI in young adult males and high hs-CRP in young adult females, these measures may not be ideal indicators of cardiovascular risk in these subgroups—which, in turn, may increase the difficulty of detecting suicide attempt-cardiovascular risk associations using these indicators.

Strengths and Limitations

The present study was the first study using the prospective-longitudinal U.S. Add Health sample to (a) examine associations among young people's suicide attempts and their young adult cardiovascular risk and (b) illuminate the roles of developmental timing, sex of the person, and source of suicide attempt exposure in these associations. Suicide attempts were measured prospectively—four times—between the ages of 12 and 32 years. Many potential covariates and confounders were assessed (socioeconomic status, health behaviors, health, depression, early adversity, impulsivity). Nevertheless, the study had several limitations.

First, most cardiovascular risks were assessed only once, and only one inflammatory marker was available. Thus, differences among inflammatory markers as well as changes in cardiovascular risk over time and directions of effects between suicide attempts and cardiovascular risk could not be examined. Suicide attempts could be motivated by poor physical health, but health declines likely only take on a greater role in the etiology of suicide attempts later in life (Sohn et al., 2014). Second, the prospective measurement of suicide attempts across four time points was a strength; nevertheless, given assessment timeframes, suicide attempts were likely missed. This would have weakened our ability to detect associations with cardiovascular risk. Third, although we controlled for many potential confounders, others were not assessed (e.g., a broader range of psychiatric disorders). Nevertheless, our findings of associations between suicide attempts and cardiovascular risk were largely consistent with those from a study that controlled for psychiatric diagnoses (Goldman-Mellor et al., 2014). Finally, to illuminate nuances in suicide attempt-cardiovascular risk associations, several statistical analyses were conducted. Our discussion focused on significant patterns of results, and the effects discussed were meaningful in size. Nevertheless our findings will need to be replicated in future research.

Conclusions

Our findings suggest that exposure to suicide attempts—one's own and others'— during the early life course signals risk for cardiovascular health problems as early as in the late twenties. Adolescent males who attempted suicide and individuals exposed to a suicide attempt in their social network may especially benefit from a dual focus on mental and physical health in care.

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