

The epidemiology of comorbid depressive and conduct disorders in early adolescence

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Abstract

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Background: Youth with both depressive disorders (DD) and conduct disorders (CD) have more impairment and worse outcomes than those with either type of psychopathology alone, yet the literature on population burden, descriptive epidemiology and unique risk factors for this form of psychiatric comorbidity is scarce. **Methods:** Using diagnostic interview data on 521 public middle school students collected annually in 6th-8th grade we estimated the period prevalence of comorbid and non-comorbid DD and CD during early adolescence and examined the sociodemographic profiles of young adolescents (YAs) in each outcome group. We tested for associations between lifetime history of stressful life events (SLEs) and psychiatric diagnosis outcome group using multinomial logistic regression. **Results:** One-third of YAs manifested one or both types of disorder over the course of middle school and one in ten experienced both. Comorbid DD/CD occurred disproportionately among YAs from racial and ethnic minority groups and single-parent households. Comorbid YAs were 3.49 (95% CI: 1.69-7.23) times as likely to have accrued 5 or more SLEs prior to middle school compared to those with neither disorder during middle school, 2.95 (95% CI: 1.06-8.20) times as likely compared to those with a DD alone and 2.89 (95% CI: 1.21-6.89) times as likely compared to those with a CD alone. **Conclusions:** Traditional approaches underestimate the burden of comorbidity during early adolescence. Future research should seek to elucidate the mechanism whereby a high burden of childhood SLEs increases the risk of early-adolescent comorbidity, so as to inform intervention strategies.

INTRODUCTION

Psychiatric comorbidity is the occurrence of two or more emotional or behavioral disorders in the same individual during the same period of time (Angold, Costello, & Erkanli, 1999). The circumstance of comorbidity between depressive disorders (DD) and conduct disorders (CD; conduct disorder and oppositional defiant disorder) in childhood and adolescence deserves special attention. From a phenomenological standpoint, DD/CD comorbidity may seem unlikely, given the phenotypic dissimilarity between manifestations of depression and misconduct. Internalizing behaviors are generally inwardly directed and often go unnoticed by others, in contrast to disruptive, overt, and attention-getting externalizing behaviors. Thus, we might anticipate that a persistently troubled young person would tend to *either* internalize their distress in the form of depression (low mood and energy, diminished interest and self-esteem, etc.) *or* express it outwardly in the form of rule-defiance, deceitfulness, aggression or destructive behavior, but not in both of these seemingly opposite ways.

Beginning with the DSM-III, recognition of this form of comorbidity was evidenced in the addition of “Adjustment Disorder with Mixed Disturbance of Emotions and Conduct”, and in the International Classification of Diseases (ICD) diagnostic system developed by the World Health Organization (WHO) that includes a childhood-specific diagnosis of Depressive Conduct Disorder (F92.0). Except for the adjustment disorder diagnosis mentioned above, the DSM-IV treats DD and CD as separate disorder classes, with no acknowledgement of the tendency for linkage between them. Mental health care providers working with children and adolescents, however, have reported that unrecognized depression often co-exists with externalizing, disruptive behavior. For example, in their document “Facts for Families”, the American Academy of Child and Adolescent Psychiatry explains, “Children and adolescents who cause

trouble at home or at school may also be suffering from depression. Because the youngster may not always seem sad, parents and teachers may not realize that troublesome behavior is a sign of depression. When asked directly, these children can sometimes state they are unhappy or sad” (Facts for Families No.4: The depressed child.).

The WHO’s acknowledgement of DD/CD comorbidity as a distinct phenomenon likely reflects the reliable observation in both community-based and clinical samples that among youth with a DD, CDs are highly prevalent, and vice versa depending on age, sex and sampling base (Wolff & Ollendick, 2006). The observed prevalence of comorbid DD/CD exceeds that to be expected by chance given the prevalence of either condition alone (i.e., the product of the individual frequencies of DD and CD) indicating that comorbidity between what are viewed as separate classes of mental illness actually follows a non-random pattern (Anderson, Williams, McGee, & Silva, 1987; Angold et al., 1999). Longitudinal research has also demonstrated that boys who develop ODD in childhood are at increased risk for both depression and disruptive behavior problems in adolescence (Burke, Loeber, Lahey, & Rathouz, 2005). The non-random co-occurrence of DD and CD suggests the possibility of common antecedents. There is evidence that DD and CD (each considered in isolation) are associated with shared exposures such as low parental socioeconomic status (SES; Rushton, Forcier, & Schectman, 2002; Boden, Fergusson, & Horwood, 2010; Rydell, 2010), instability in family structure (Rushton et al., 2002; Boden et al., 2010; Rydell, 2010), parental depression (Singh et al., 2011; Kim-Cohen, Moffitt, Taylor, Pawlby, & Caspi, 2005), exposure to violence (Boden et al., 2010) and other forms of trauma such as childhood sexual abuse (Fergusson, Boden, & Horwood, 2008).

Comorbid DD/CD appears to reflect a more severely impairing form of psychopathology than DD or CD alone. Compared with non-comorbid DD and CD, youth comorbidity is

associated with both an earlier onset of alcohol disorders (Rohde, Lewinsohn, & Seeley, 1996) and a greater likelihood of alcohol-related problems by young adulthood (Pardini, White, & Stouthamer-Loeber, 2007). Depressed youth with co-occurring disruptive behavior problems show lower response to medication than those with other concurrent disorders (Hughes et al., 1990) and are more likely to attempt suicide than those with DD alone (Lewinsohn, Rohde, & Seeley, 1995; Fombonne, Wostear, Cooper, Harrington, & Rutter, 2001; Vander Stoep et al., 2011). Compared to either DD or CD alone, comorbidity in childhood has also been found to increase the risk of later criminality (Sourander et al., 2007) and high social service utilization (McCrone, Knapp, & Fombonne, 2005), both of which are clearly tied to financial and social burden on communities. Adding another interesting piece of evidence to the “severity hypothesis” of comorbidity, Sellers and colleagues (Sellers et al., 2013) have demonstrated that psychiatric comorbidity in depressed mothers increases the risk of incident psychopathology in their adolescent children in a dose-response fashion, such that the higher the number of comorbidities in the mother, the higher the risk of new-onset offspring disorder.

There remain a number of important gaps in our understanding of the population distribution and determinants of comorbid DD/CD. While recent evidence estimates that the median age of onset is 11 years for behavior disorders and 13 years for mood disorders (Merikangas et al., 2010), it is unknown how commonly DD and CD co-occur in the general population during the critical developmental period of early adolescence. Also, despite the antecedents shared in common by DD and CD, there is a paucity of literature on how young people with comorbid DD and CD differ from their peers who meet criteria for DD or CD alone, both in terms of sociodemographic characteristics and prior exposures and life experiences – knowledge that could have implications for prevention, identification and treatment. In their recent review of the

state of the literature on the distribution of, and exogenous risk factors for, psychiatric comorbidity, Cerda and colleagues (Cerda, Sagdeo, & Galea, 2008) concluded that more research is needed on the key risk factors for clustering of psychopathology, given the significant personal burden created by comorbid disorders and their high prevalence across populations.

One characteristic that may differentiate youth with comorbid DD/CD from those manifesting symptoms of only one of these disorder categories is past burden of stressful life events (SLEs). There is a robust literature documenting the etiologic association between SLEs and psychopathology (including depression and, less frequently, conduct disorders) in children and adolescents, with evidence found for a complex array of biological, developmental, psychological and social mechanisms underlying the causal connection (see Hammen, 2005)(and Grant, Compas, Thurm, McMahon, & Gipson, 2004 for comprehensive reviews). For example, repeated exposure to stressors has been shown to impair hypothalamic-pituitary-adrenal (HPA) axis regulation(Sapolsky, 1994); the resulting state of excess in circulating glucocorticoids and chronic activation of the amygdala, termed “allostatic load” (Schulkin, McEwen, & Gold, 1994), is experienced as sustained negative affectivity and chronic anticipation of negative events (Bradley, 2000), p. 85. Additionally, dysregulation of the HPA axis appears to interfere with attention, focus and new memory formation, presenting in affected children as impaired behavioral self-regulation (Gunnar & Barr, 1998).

Following from Rutter’s (Rutter, 1989) demonstration of the additive effects of the number of stressors on the likelihood of developing psychopathology, we hypothesize that adolescents with comorbid DD/CD will evidence a higher cumulative burden of childhood SLEs than those with just one of these disorders, who in turn will have experienced more SLEs than those with neither disorder. Since it known that stress begets stress (Bradley, 2000, p.82), and that

psychopathology itself precipitates stress (Grant et al., 2004), a probable pathway to comorbidity is via early childhood SLEs which induce disruptive behavior, which in turn catalyzes additional (or the perpetuation of) SLEs, leading to a layering of depression on top of misconduct. For example, Nobile et al. (Nobile et al., 2013) reported that, in their longitudinal study of psychopathology and adversities in a general population sample recruited in preadolescence, mediation analyses confirmed that SLEs account in part for the continuity of conduct problems into adolescence, in addition to the progression to affective problems. The reverse ordering of depression and misconduct in this pathway is also plausible. Models of gene-environment interplay have also been used to illustrate how adversities can both perpetuate and be a consequence of existing disorders (Mash & Barkley, 1996).

In moving forward with this line of inquiry, it is important to think critically and explicitly about how comorbidity is defined, since measurement methods and a classification system ill-fitted to the phenomenon may lead to invalid results. Past studies of depression and misconduct comorbidity among children and adolescents have often required that criteria for both types of condition be met simultaneously – a cross-sectional approach - or that both conditions persist over two assessments – a dual growth trajectory approach (Vander Stoep et al., 2012; Diamantopoulou, Verhulst, & van der Ende, 2011; Chen & Simons-Morton, 2009; Wiesner & Kim, 2006). These characterizations fail to account for the episodic nature of depression or the diverse forms that comorbidity may take in early adolescence, including the potential for individual and sex-specific variation in order, age of onset, and relative latency and trajectories of the component disorders. As such, these traditional approaches may be biased towards ascertainment of the most severe and/or longstanding cases of DD/CD comorbidity, failing to capture among the comorbid those youth who, in a cumulative sense, manifest the requisite

diverse manifestations of symptomatology within a developmentally coherent period of time, but who did not happen to do so at the exact point when the “snapshot” was taken. We argue that the accuracy of ascertainment of comorbidity at this stage of development is improved by use of a period prevalence approach in which DD and CD may present either simultaneously or sequentially within a specific developmental window. In such a period prevalence approach the case definition of comorbidity is to meet criteria for each of the relevant disorders at some point within a given window of time. Variations on this approach are seen in more recent literature examining the distribution and determinants of psychiatric conditions, for example Farmer and colleagues’ “lifetime (to age 24 years) disorder aggregation approach” (Farmer, Kosty, Seeley, Olino, & Lewinsohn, 2013), and Kessler and colleagues’ “lifetime (to mid-adolescence) comorbidity” method (Kessler et al., 2012). Furthermore, for purposes of anticipating supportive services, we argue that it is important to view the burden of health problems across developmentally coherent periods of time, rather than on the basis of prevalence estimates taken at a moment in time.

In this paper we present the descriptive epidemiology of comorbid DD/ CD in early adolescence and investigate whether comorbid DD/CD presenting during early adolescence is associated with childhood exposure to a high number of SLEs, relative to DD or CD alone. The specific aims of the present study were threefold: 1) to estimate the prevalence of comorbid and non-comorbid DD and CD over the three year period in early adolescence corresponding to middle school enrollment in a population-based cohort, 2) to compare the sociodemographic profile of young adolescents (YAs) with comorbid DD/CD to those with a non-comorbid DD or CD, and 3) to evaluate whether, in comparison with peers who have one component disorder or no disorder, comorbid YAs have higher lifetime burden of SLEs.

MATERIALS AND METHODS

Sample

The Developmental Pathways Project (DPP) is a population-based, prospective cohort study of the phenomenology, antecedents and outcomes of internalizing and externalizing psychopathology in adolescents. Participants were recruited from four public middle schools in Seattle, Washington, USA. Schools were selected from distinct geographic areas of the city such that the sample would represent the racial, ethnic and socioeconomic diversity of the Seattle Public School District population.

Beginning in autumn 2001, four consecutive annual cohorts of sixth-grade students (mean age 12.02 years, $SD = 0.43$) underwent universal screening for depressive and conduct problems soon after entering middle school (stage 1). Of the almost 3,000 students in the sampling frame, a total of 2,187 were screened. Each year, a stratified random sample of screening participants, with oversampling of those with elevated scores on these dimensional measures of depressive and/or behavioral problems, was enrolled into the longitudinal phase of the study (stage 2), which consisted of five waves of assessments conducted at approximate six-month intervals during middle school (Waves 1-5), a ninth grade assessment (Wave 6) and another at twelfth grade (Wave 7). The present analyses utilize data collected at Waves 1 (baseline), 3 and 5 (Figure 1).

Measures

Depression and conduct disorders.

We used a novel approach to ascertaining comorbidity that acknowledges both the clinical relevance of categorical diagnosis and the reality that disorder manifestation is episodic in

nature: we classified a participant as comorbid if s/he evidenced both depressive and conduct disorders at some point over the middle school assessment period, regardless of whether the disorders appeared concurrently or sequentially. This approach acknowledges that young adolescents at varying stages of pubertal development have a broad repertoire of cognitive and behavioral manifestations of emotional distress that differ from those of adults in both their quality and stability over time.

To ascertain DD and CD via this approach, we administered the Depression, Conduct Disorder and Oppositional Defiant Disorder modules of the Computerized Diagnostic Interview Schedule for Children, version IV (CDISC-IV) to each participant and his/her primary caregiver approximately one year apart in 6th, 7th, and 8th grades (Waves 1, 3 and 5, respectively). For these analyses we used the past-year, combined caregiver/youth diagnosis to maximize sensitivity for detecting disorder, since depression (especially cognitive symptoms) is better detected by self-report (Cole et al., 2002), whereas conduct problems are better detected by caregiver report (Achenbach, McConaughy, & Howell, 1987). The algorithm used to create the combined diagnosis considers a diagnostic criterion present if it is endorsed by either of (or both) the youth and caregiver.

A participant was classified as DD-only if at some point during middle school s/he met criteria for past-year major depression, minor depression or dysthymia but never any conduct diagnosis (American Psychiatric Association, 2000; See Appendix A for diagnostic criteria). Similarly, the CD-only group was composed of those who met criteria for past-year conduct disorder or oppositional defiant disorder at one or more of the three annual CDISC-IV assessments, but never any depression diagnosis. The comorbid DD/CD group comprised participants who received both DD and CD diagnoses either concurrently or sequentially (at the

same or different interviews) over that three-year period. Finally, participants were classified as having neither type of disorder over middle school (NE) if they did not meet criteria for past-year depressive or conduct disorders at the any of the relevant interviews.

Sociodemographic factors.

Participants' caregivers completed a demographic questionnaire at baseline (Wave 1). For these analyses we used the following sociodemographic variables, categorized as described: annual household income ($\$ < 25,000$ vs. $\geq \$25,000$), parental nativity (both US-born vs. at least one foreign-born), maternal educational attainment (high school/GED or less vs. post-secondary), and number of adults in the household (one vs. two or more). Participant race (African American, Asian/Pacific Islander, Caucasian or Native American), ethnicity (Hispanic vs. Non-Hispanic) and sex (male vs. female) were obtained from school district records.

Stressful life events.

Caregivers completed the Life Events Checklist (Johnson & McCutcheon, 1980) at baseline. This measure has been found to be reliable and valid for child populations in the United States (Johnson & Sarason, 1979). For each of 22 items (e.g., "a new baby brother or sister was born into (participant's) family", "(participant) moved to a new home", "somebody close to (participant) died", "(participant's) parents got divorced or separated"), caregivers were asked to report whether the youth participant had experienced the event in their lifetime and whether the event had a positive or negative effect on the youth. Negative-impact life events are referred to as SLEs in this paper. The number SLEs reported to have occurred was summed for each participant, and this total score was dichotomized into low (0-4 events) vs. high (5 or more events). Five events represented the best central split in this sample, as 43% had experienced five or more events.

Analysis

All statistical analyses were conducted using Stata Version 11.2 for Windows (StataCorp, College Station, TX). To account for over-sampling of YAs who screened high for depression and conduct problems and to make the sample demographically similar to the Seattle public middle school population, two-component weights were derived and applied to analyses. The first component was a sampling fraction weight that was equivalent to the inverse probability of being enrolled based on the representation of the four groups (low depression score/low misconduct score, high depression score/low misconduct score, low depression score/high misconduct score, high depression score/high misconduct score), in the stage 1 universal screening sample. The second component was a post-stratification weight that accounted for differences in gender, race/ethnicity, and educational program (e.g., regular, gifted, special education, English Language Learner), between the screening and longitudinal study samples. These two weights were multiplied to produce the final weight for each individual.

Statistical Analyses.

We tabulated the proportion of YAs in each outcome group (comorbid DD/CD, DD alone, CD alone, and neither) to estimate the middle school period prevalence of comorbid and non-comorbid depressive and conduct disorders in the Seattle public school population, both overall and for males and females, separately. The multiple imputation package of commands in Stata does not support the use of Pearson chi-square tests, suggesting in lieu multinomial logistic regression. To test the null hypothesis of no difference in the distributions of membership in these four outcome groups between males and females, we ran multinomial logistic regression using sex as the independent variable and group membership as the dependent variable; the F-

test reports whether this model is significantly different from what would be expected under the null hypothesis.

Comparisons of the proportion belonging to each outcome group by sociodemographic factors were performed to evaluate whether YAs with comorbid DD/CD had a distinct profile. Because simple chi-squared tests of independence for categorical variables cannot be performed across multiply imputed datasets, we used the F-test from bivariate multinomial logistic regression to assess whether there were overall differences in outcome group status by these factors. We then tested for associations between lifetime history of negative life events and psychiatric diagnosis outcome group using multinomial logistic regression to estimate odds ratios (OR). First, comparisons were made using the “neither disorder” outcome as the reference to estimate whether being diagnosed with a DD alone, a CD alone or both disorders was associated an increased odds of high negative life event burden. Then two more comparisons were made, using DD only and CD only as the reference groups, respectively. These ORs are interpreted as the ratio of the odds of a high burden of negative life events to the odds of low burden, comparing YAs with comorbid DD/CD to those with a DD alone or CD alone, depending on the comparison. Comparisons with both single-disorder and no disorder groups were made in order to determine whether a high burden of SLE was associated similarly with all manifestations of early adolescent psychopathology, or whether the association was particularly strong with comorbid manifestations.

We assessed the following potential confounders were associated with both exposure and outcome: sex, race, ethnicity, income, number of adults in the home, parent nativity, and parent educational attainment. Only race and number of adults in the home were found to be associated with both SLE burden and psychiatric diagnosis group, thus adjusted estimates are presented

based on models including these confounders. For descriptive purposes we also tabulated the number of negative life events for each psychopathology group using the non-imputed data (see below).

Missing data.

Combined caregiver/youth CDISC diagnoses were complete for 521 participants (100%) at Wave 1, 446 youth (85.6%) at Wave 3, and 447 youth (85.8%) at Wave 5. Due to missing CDISC diagnoses at one or more interviews, the middle-school psychopathology group for 93 (17.9%) participants was indeterminate (for example, if a YA had major depression at Waves 1 and 3 but was missing at Wave 5, their group assignment would have been DD if Wave 5 diagnosis was none or DD, but comorbid DD/CD if a CD was detected).

To account for missing data in the least biased manner and to maintain sample size, we used multiple imputation to substitute non-missing plausible values for missing values (Raghunathan, 2004; Graham, 2009). Valid inference using imputed data requires the assumption that data were missing at random after accounting for observed variables. The fact that proportions of missing data at each study visit were similar across the categories of stage 1 screening symptom group, negative life event burden, and other participant characteristics suggests that this assumption was not violated (Table 1). Multiple imputation was performed using imputation by chained equations (ICE) (Royston, 2005). Imputed data were derived based on regression models that included Wave 1, 3 and 5 past-year, combined diagnoses (major depression, minor depression, dysthymia, conduct disorder, oppositional defiant disorder), youth sex, ethnicity, parental nativity, stage 1 screening symptom group and baseline Medicaid status. Analyses were performed across the 10 imputed data sets, and results were combined such that parameter

estimates and their standard errors reflected the uncertainty of the imputed values (Rubin, 1987). All reported results represent the weighted, multiply-imputed analyses unless otherwise noted.

RESULTS

Description of the sample

A total of 272 boys (52.2%) and 249 girls (47.8%) enrolled in the DPP longitudinal study at Wave 1 (Table 1). The mean ages for completers of Waves 1, 3 and 5 were 12.0, 13.0 and 14.1 years, respectively. The enrolled sample was 89.1% US-born; 31.1% had at least one foreign-born parent. Annual household income was distributed across the low and middle income range, with over a quarter (26.7%) reporting under \$25,000 and almost a third (31.1%) reporting \$75,000 or greater; 27.6% were Medicaid-enrolled. Participants' primary caregivers were generally well-educated, with almost half (48.2%) having attained a Bachelor's degree or higher, and another 28.4% having completed some post-secondary school. In terms of household composition, over a quarter (27.3%) of participants resided with a single adult, there were most often two children under 18 years of age in the home (44.9%), and only 23 participants (4.4%) did not live with family in the six months prior to Wave 1.

The ethnic and racial distribution of the sample (4% American Indian, 28% African American, 16% Asian, 3% Pacific Islander and 49% Caucasian; 10% Hispanic ethnicity) is generally representative of students enrolled in Seattle Public Schools. Among all regular and alternative public middle schools in the 2004-2005 school year, for example, the student body was 3% American Indian, 23% African American, 23% Asian/Pacific Islander, 40% Caucasian and 12% Chicano/Hispanic (Seattle Public Schools, November 2005).

Period prevalence of comorbid depressive disorders and conduct disorders

The three-year middle school period prevalence of comorbid depressive and conduct disorders was 9.5% (95% CI: 6.5-12.4). By comparison, wave-by-wave, “snapshot” estimates of past-12-month prevalence of comorbid DD/CD were 2.5% (95% CI: 1.3-3.4) at Wave 1, 5.5% (95% CI: 2.7-8.4) at Wave 3, and 3.9% (95% CI: 1.3-6.5) at Wave 5. For depressive disorders (with or without a conduct disorder) these figure were 8.7% at Wave 1, 8.2% at Wave 3, and 7.6% at Wave 5; for conduct disorders (with or without a depressive disorder) the 12-month period prevalence was 14.5% at Waves 1 and 3 and 13.2% at Wave 5.

An estimated one-third of youth met criteria for a depressive (DD) and/or a conduct disorder (CD) over this developmental period. The middle-school period prevalence of depression (with or without a conduct disorder) was 22.2% (95% CI: 18.4-26.0); with 10.2% (95% CI: 6.6-13.9) meeting criteria for a DD only. Over this time period, 24.3% (95% CI: 20.0-28.6) of YAs met criteria for a conduct disorder, with or without depression; 14.9% (95% CI: 11.2-18.5) met criteria for CD only. Of YAs with a diagnosis of depression at some point over middle school, almost half (48.9%) also had a CD during that period. Similarly, of those with a conduct disorder, 45.3% also manifested a DD.

Descriptive Epidemiology of Comorbid Depressive and Conduct Disorders

Sex, race and ethnicity.

For boys, the estimated three-year period prevalence of comorbid disorders was 10.7% (95% CI: 5.9-15.5) and, for girls, it was 8.1% (95% CI: 4.8-11.5). The overall distributions of psychopathology group membership did not differ significantly by sex ($F(3, 399.1)=1.80$, $p=0.146$). The sex-specific estimates of the period prevalence of depression (with or without

conduct disorder) were 22.5% (95% CI: 15.8-29.1) for boys and 16.7% (95% CI: 11.1-22.4) for girls. The estimated overall period prevalence of conduct disorders (with or without depression) was 28.4% (95% CI: 21.9-35.0) for boys and 19.9% (95% CI: 14.2-25.6) for girls.

Table 2 illustrates comparative distributions of sociodemographic characteristics of the YAs with comorbid DD/CD compared to other psychopathology groups. The distribution of the four cumulative psychopathology outcome groups varied significantly by race [$F(6,441.4) = 2.30, p = 0.034$]. Specifically, compared to the racial composition of the source population, the DD/CD group was comprised of an over-representation of Black and Native American YAs, the CD group contained an over-representation of Whites, and the DD group was composed of an over-representation of Blacks. Variation in psychopathology group composition by Hispanic ethnicity approached statistical significance [$F(3, 466.9) = 2.43, p = 0.065$]: the estimated period prevalence of comorbid DD/CD was three times higher among Hispanics than non-Hispanics, whereas that of non-comorbid DD was doubled in non-Hispanics compared to Hispanic YAs. The period prevalence of non-comorbid CD appeared similar between Hispanic and non-Hispanic YAs.

Other socio-demographic characteristics.

Psychopathology outcome group distributions did not vary significantly by annual household income [$F(3,423.8) = 1.84, p = 0.139$], primary caregiver educational attainment [$F(3,344.8) = 0.73, p = 0.535$], or parental nativity [$F(3,455.1) = 0.71, p = 0.544$]. On the other hand, the number of adults in the home was associated with group membership [$F(3,423.0) = 2.66, p = 0.048$]: of particular note, the estimated period prevalence of comorbid DD/CD among YAs in a single-caregiver household (15.1%) was twice that of YAs with two or more adults at home (7.6%).

Association between stressful life events and comorbidity

Figure 2 shows the distribution of SLEs by psychopathology group. The middle school period prevalence of comorbid DD/CD among YAs who had accumulated five or more SLEs by 6th grade was 15.7%, compared to 5.3% among those with fewer than five (Table 2). Multinomial logistic regression results revealed that YAs with five or more SLEs did not have a statistically significantly increased odds of DD alone (OR = 1.18, 95% CI: 0.53-2.66) or CD alone (OR = 1.21, 95% CI: 0.68-2.14) during middle school, but did have a significantly increased odds of comorbid DD/CD over this period (OR = 3.49, 95% CI: 1.69-7.23) using those with neither diagnosis as the reference group (Table 3). Over the course of middle school, YAs who had experienced a high burden of negative life events had an estimated three-fold increased odds of comorbid DD/CD even when compared to those with either DD alone (OR = 2.95, 95% CI: 1.06-8.20) or CD alone (OR = 2.89, 95% CI: 1.21-6.89) (Table 4). Multivariate analyses adjusting for race or number of adults in the home did not change the estimated associations appreciably (Tables 3 and 4).

DISCUSSION

In this school-based study we found that about one in ten young adolescents met diagnostic criteria for both a DD and a CD over the three-year course of middle school, and further, that prevalence estimates were similar for girls and boys. We also found that approximately one in ten middle-school youth experienced a non-comorbid DD over this period, while the cumulative burden of non-comorbid CD in this population was slightly higher at approximately one in seven. Thus, greater than a third of YAs exhibited clinically diagnosable levels of depression or conduct problems or both over the course of the three-year middle school period.

The traditional method for measuring the burden of psychopathology in a population is to take a single prevalence “snapshot”. This approach is often used in population-based studies, as for example in the National Comorbidity Survey Adolescent Supplement (Merikangas, Avenevoli, Costello, Koretz, & Kessler, 2009), but its sensitivity and reliability have been questioned (Cole et al., 2002). When applied to the question of how common it is for young adolescents to exhibit two forms of psychopathology, in a longitudinal study, however, it may be preferable to relax the requirement that the two forms of psychopathology occur simultaneously. In using a wider, yet still developmentally coherent, case ascertainment window, we were able to account for the episodic presentation and varying phenotypes of depressive and conduct disorders in early adolescence. Indeed, our results demonstrate that comorbid DD/CD classified on the basis of simultaneous expression of both disorders underestimates the burden of comorbid psychopathology in this development stage.

Our approach to defining young adolescent DD/CD comorbidity used three annual past 12-month assessments and relaxed the requirement that diagnostic criteria for each of the contributing disorders be met during the same assessment. When the traditional approach to ascertaining comorbidity was applied, we estimated a past-year prevalence of comorbid DD/CD of under 6% at each annual assessment (range: 2.5% to 5.5%), underestimating considerably the population burden of co-occurring DD and CD in early adolescence of 9.4% ascertained using the new approach. Seventy percent of youth classified as comorbid had at least one assessment at which they met criteria for only a DD or a CD alone, and 47.4% had at least one assessment at which they met criteria for neither type of disorder, which further shows how comorbidity burden within early adolescence is underestimated when single assessments are used for case ascertainment. All but 15.8% who manifested both a DD and a CD during this

period met criteria for both diagnoses simultaneously at one or more of the three assessments, while only one participant who developed comorbid DD/CD over the course of middle school met criteria for both a DD and a CD across all three assessment waves.

Using the three-year period prevalence approach yielded interesting insights into the burden of non-comorbid disorders, as well. We observed, for example, a past-year depressive disorder prevalence of approximately 8% at each of the Wave 1, 3 and 5 assessments, but by employing the three-year prevalence approach, we discovered that it was not the same 8% who were depressed during each year, with the full population burden of depression in early adolescence, estimated at a much higher 22.2%.

Comparison of these findings to prior literature of the prevalence of comorbidity in early adolescence is not straightforward due to methodological differences. For example, past studies have differed by ascertainment of depression and conduct problems using dimensional measures with various cut-points for categorizing youth (e.g., 0.5 SD above the mean for that sample) or an earlier version of the DSM; classification of youth based on a cross-sectional snapshot, lifetime prevalence assessed retrospectively or group membership trajectory over time (initially comorbid and remains comorbid, initially conduct problems only then depression also develops, etc.); sampling from clinically-referred populations, different age groups or a single sex.

In the National Comorbidity Survey Replication – Adolescent Supplement (NCS-A), among 3,870 13-14 year olds the reported lifetime prevalence (weighted to the population distribution of selected sociodemographic and geographic variables) was 8.4% (SE 1.3) for major depressive disorder or dysthymia, 12.0% (SE 1.2) for ODD, 4.4% (SE 1.2) for CD, and 9.2% (SE 1.0) for any two disorder classes (Merikangas et al., 2010). This study was similar to ours in its use of non-clinical sampling frame, sex distribution, and DSM-IV diagnostic criteria obtained via

interview, though they required the criterion of significant distress or impairment associated with symptoms, whereas the DISC scoring algorithm we used does not. This latter difference would have lead us to expect that their observed prevalence estimates would be lower than ours given the stricter criteria, except that they ascertained lifetime disorder prevalence, whereas we sought to estimate the burden experienced during early adolescence only, and their classification of comorbidity included other disorder classes that we did not assess, including eating, anxiety and substance use disorders; both these latter two differences would lead to higher estimates compared to our study. While retrospective ascertainment of age of onset in the NCS-A suggested that risk of mood and behavioral disorders was fairly low in childhood and began to rise steadily in early adolescence, it is not possible to discern from their data what proportion of the population was estimated to manifest a DD and/or a CD during early adolescence, specifically, as an unknown fraction who experienced disorders earlier in childhood would not continue to have them during early adolescence.

In another non-clinical sample, Chen and Simons-Morton (Chen & Simons-Morton, 2009) assessed conduct problems and depression longitudinally in five waves from sixth to ninth grade among 2,453 Maryland middle-school students in the context of a school-randomized intervention to prevent substance use and antisocial behavior. Respondents were categorized into psychopathology trajectory groups based on patterns over time in symptom scores on self-administered questionnaires using general growth mixture modeling; the authors reported that 8.8% of boys and 3.7% of girls belonged to the high conduct problem+high depression symptom score group. These estimates are slightly lower (particularly for girls) than the ones we obtained, likely as a result of several methodological differences. Three potential sources of discrepancy of note were that a) conduct problem assessment did not capture some of the less severe behavior

problems reflective of ODD, but rather was weighted towards evidence of aggression as manifested in CD, b) the sensitivity for detecting depression and, even more so, conduct problems was likely lower as it was based solely on young adolescent self-report, whereas we took into account caregiver report, and c) use of the trajectory classification paradigm may render prevalence estimates that differ in ways that are difficult to predict.

A third population-based study – the Great Smoking Mountains Study (GSMS) – investigated the development of psychiatric disorders and mental health service needs using an accelerated cohort¹ of boys and girls from western North Carolina recruited between ages 9 and 13 and followed approximately annually to age 16. Using interviewer-based assessment of past-three-month DSM-IV diagnoses using combined youth and parent report with The Child and Adolescent Psychiatric Assessment (CAPA), the study estimated that the cumulative prevalence from age 9 to 16 was 9.5% (SE 1.1) for any depressive disorder, 9.0% (SE 1.2) for conduct disorder and 11.3% (SE 1.0) for ODD (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003). These estimates are lower than the ones we obtained, which may be attributable in part to use of past-three-month disorder ascertainment in the GSMS, compared to past-year ascertainment in our study, however the period over which disorder could be accumulated in GSMS was up to seven years, compared to only three years in our study. The authors did not report the point or cumulative prevalence of comorbidity, but rather quantified comorbidity via odds ratios reflecting the magnitude of the association between pairs of disorder classes at a given assessment, pooled over all waves. For example, they reported that the odds of past-three-month depressive disorder were 21.3 times higher among girls with past-three-month conduct disorder

¹ In an accelerated cohort design, one samples multiple age cohorts and then collects longitudinal data on members of each cohort. This permits study of age-outcome trajectories over a broad age span during a study of short duration.

compared to those without (5.0 times higher for boys), and that the odds of past-three-month depressive disorder were 15.1 times higher among girls with past-three month ODD compared to those without (20.7 times higher for boys).

Finally, Anderson et al.'s (Anderson et al., 1987) study of a birth cohort in Dunedin, New Zealand, estimated that the prevalence of co-occurrence between conduct disorder and depression (using DSM-III criteria) was between 1.5-2.9% among 11 year-olds. This is very close to our estimate of the "snapshot" prevalence of comorbid DD/CD at Wave 1, which was 2.5%.

Results addressing our second aim suggest that young adolescents meeting criteria for both a DD and a CD during middle school appear to differ sociodemographically from peers accruing a DD or a CD alone or neither disorder. Descriptively, the comorbid DD/CD group tended to be characterized by disproportionate representations of Black, Native American and Hispanic youth and of those with a single caregiver. Furthermore, comparison of demographic characteristics did not suggest that YAs with comorbidity share consistent similarities with depressed youth or those with conduct disorders, but rather that they were over-represented by Black and single-caregiver youth like the DD-only group, and were over-represented by Native American youth like the CD-only group (Table 5). While male sex was associated with conduct disorder alone, it was not associated with DD/CD comorbidity.

There are no prior studies to which to compare our findings regarding the sociodemographic profile of young adolescents with comorbid DD/CD. The NCS-A study (Merikangas et al., 2010) reported that depressive disorders were more common among females, Hispanics (vs. Non-Hispanic white), youth with married or cohabiting parents (vs. never married) and those whose parents had less than college education, and that behavior disorders (which included attention-

deficit hyperactivity disorder in addition to CD and ODD) were more common among males, youth with divorced or separated parents, and those whose parents were not college-educated. The only similarities between these findings and ours were the associations between caregiver education and depression and Hispanic ethnicity and depression, and sex and conduct disorders, though the validity of any comparison is undermined by numerous differences in methodology, as were mentioned above, as well as the pooling of all ages 13-18 and use of multivariate logistic regression for assessing sociodemographic correlates, and the lack of examination of sociodemographic predictors of comorbidity per se in the NCS-A analysis.

The results of our analyses confirmed our hypothesis that exposure to a high lifetime burden of SLEs differentiates young adolescents with comorbid DD/CD not only from NE peers but also those with non-comorbid DD or CD. Young adolescents with DD/CD were 3.5 times as likely as those with neither disorder type to have experienced five or more SLEs. A similar pattern was observed when comparing YAs with DD/CD to those with a single component disorder: a history of five or more SLEs was 2.9 times more common among youth with DD/CD than among peers with either a DD only or a CD only.

While it is well-established that SLEs are a common antecedent of both depression and conduct disorders (e.g., Low et al., 2012; see Grant et al., 2004 for a review), very little prior work has examined the association between SLE burden and the co-occurrence of these disorder classes. One study conducted among 16-17 year-old high school students in Uppsala, Sweden reported that adolescents with a lifetime history of comorbid depression and conduct disorder (per diagnostic interview with the youth only) had experienced significantly more stressful life events than age-, sex- and school class-matched controls and had a higher mean number of events than peers with non-comorbid depressive disorder (Olsson, Nordstrom, Arinell, & Von

Knorrning, 1999). Despite differences in population and method of case ascertainment, these findings are in line with ours. Another study conducted in Barcelona, Spain, examined risk factors distinguishing clinically-referred adolescents aged 8-17 years currently meeting DSM-IV criteria for non-comorbid DD or non-comorbid CD from those meeting criteria for a DD or a CD, based on combined youth/parent report (Ezpeleta, Granero, & Domenech, 2005). Stressful life events not under the control of the youth occurring prior to the last year were ascertained using the youth-report of the Life Events Checklist (Johnson & McCutcheon, 1980). The authors found that the total number of SLEs was associated with a significantly increased risk of comorbidity, when compared to non-comorbid DD but not in reference to non-comorbid CD (they did not describe how they categorized and parameterized SLEs, but did report controlling for sex, age and other comorbid psychiatric disorders). Thus, the limited prior work in this area is partially consistent with our finding of a particularly high burden of SLEs in adolescents with comorbid DD/CD.

There are a number of reasons why a high burden of SLEs could increase the risk of comorbid DD/CD in early adolescence. Repeated exposure to stressors impairs neuroendocrine function of the HPA axis in a manner that has been shown to impact both affect and behavior regulation (Gunnar & Barr, 1998; Bradley, 2000). The experience of both affective and behavioral dysregulation could manifest phenotypically as depressed mood and disruptive behavior. Impairment of neuroendocrine function could affect behavior and affect regulation simultaneously or sequentially. In an expansion on Capaldi and Stoolmiller's (Capaldi & Stoolmiller, 1999) "failure model" – noxious conduct causes social and academic maladjustment, which in turn results in increased risk for depression – exposure to SLEs could, in some children, lead to oppositional or antisocial conduct, which tends to cause additional stressors taking the

form of academic and/or social difficulties (with family, peers or authority figures). These resultant difficulties are themselves stressors and are markers of maladjustment with one's environment, which can lead to the layering of depression on top of disruptive behavior. One limitation of our study was that we lacked data on timing of first onset of behavioral and emotional difficulties, which may have been prior to the first study assessment, so we were unable to empirically assess whether the failure model explains the mechanism whereby the childhood history of a high burden of SLEs is associated with early adolescent DD/CD comorbidity.

There are several strengths to our study design. First, we were able to capture cumulative psychopathology burden across a developmentally coherent period representing early adolescence, rather than taking a single point-in-time snapshot. While use of longitudinal approaches can induce its own internal validity concerns due to missing follow-up data, our participant attrition was low across interview waves and did not appear to be associated with SES markers, SLEs or baseline depression or conduct problems. Therefore it is reasonable to consider the missing data "missing at random", rendering our use of multiple imputation valid. Second, we minimized the misclassification of participants' diagnostic status by using both youth and caregiver past-year report at one-year intervals. Third, we partitioned both youth with a depressive disorder and those with a conduct disorder into comorbid and non-comorbid subgroups, which permitted us to evaluate the distinctiveness of comorbid DD/CD in comparison to single-disorder reference groups. Fourth, our use of a non-clinical sample and demographic weighting yielded results that generalize to a general population of public middle school students.

The results of this study should be considered in light of its limitations. The first is the possibility of errors in ascertainment of exposure to SLEs. Classification of exposure groups was based on caregiver endorsement of a specific set of events contained in a checklist. Thus, SLEs not appearing on the list would not be counted towards the total. In addition, each rating reflects the idiosyncratic meaning of the event to the respondent and their subjective perceptions of the valence and strength of the event's impact on the adolescent (Hammen, 2005). Finally, there is some evidence that psychiatrically impaired mothers systematically over-report emotional and behavior problems in their children (Boyle & Pickles, 1997; Najman et al., 2001; Milne et al., 2009). While we were unable to find evidence in the literature that caregivers' mental state biases their report of the child's history of SLEs, this is conceivable given evidence of biased reporting of child mental health and behavior. Thus, to the extent that caregiver respondents with mental health problems were more common among the comorbid DD/CD group, differential misclassification of SLE exposures may have occurred, biasing the estimate of the association upwards. We were unable to conduct sensitivity analyses to assess the presence and impact of such potential bias on our results due to a lack of data on caregiver respondent psychological characteristics at the time of the relevant assessment.

Second, our diagnostic interview data (CDISC) assessed psychopathology over the preceding 12 months, so we were not able to capture diagnostic status prior to one year preceding the Wave 1 assessment. As such we were unable to differentiate between incident (first episode), prevalent and recurrent manifestations of depressive and conduct disorders among those identified over the follow-up period. Among comorbid DD/CD cases, we are also unable to determine the lifetime developmental sequence of classes of disorders, due to the same data limitation.

Our finding of a robust association between a high burden of past SLEs and comorbid DD/CD during early adolescence is consistent with a model positing that an increased risk of comorbid DD/CD results from exposure to a high burden of SLEs. However, youth may have had episodes of depression and/or conduct problems prior to middle school, such that we can't rule out the alternative model in which the experience of a higher than normal number of SLEs could be a consequence of earlier depression, conduct disorders or comorbid psychopathology. Our data are also consistent with a dynamic, bidirectional model of the stress-comorbidity association. Despite our inability in this study to evaluate the validity of each of these models, the finding of an increased likelihood of experiencing both a DD and a CD over the course of early adolescence (whether new onset, recurrence, or continuation from childhood) given a high past burden of SLEs remains useful from the practical standpoint of school-based mental health needs assessments and primary care mental health screening of young adolescents.

In future investigations utilizing this longitudinal cohort we aim to validate our novel period prevalence approach to defining early adolescent comorbidity by studying outcomes of YA's in academic, interpersonal and physical and mental health domains of YAs classified as comorbid via the period approach to those of YAs classified on the basis of having two diagnoses simultaneously. We also plan to investigate further the types of SLEs reported, assessing whether those of youth with DD/CD differ qualitatively from SLEs reported to have been experienced by peers in the DD-only, CD-only and NE groups.

Early adolescence is a critical juncture in the transition from childhood to adulthood, a potential turning point when earlier psychologically-based problems can resolve, continue, or become amplified homo- or heterotypically. In this paper we have demonstrated that one in three young adolescents will experience a depressive and/or conduct disorder over the three-year

course of middle school, and that one in ten will experience both. In addition, we found that this comorbidity occurs disproportionately among YAs from racial and ethnic minority groups and single-parent households. Finally, we showed that a high burden of stressful life events prior to middle school is associated with heterotypic comorbidity and that this exposure distinguishes comorbid YAs not only from peers with no disorder over middle school, but also from those with either depression or conduct disorder alone. The transition from elementary to middle school offers an opportunity for intervention with vulnerable youth to mitigate the effects of childhood stresses and the future burden of psychopathology and negative outcomes associated with comorbid depression and conduct disorders.

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DEDICATION

I dedicate this work to all adolescents struggling with mental illness, and to my husband, who has been my steadfast supporter during my thesis journey.

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FIGURES AND TABLES

Figure 1: Study Design Timeline

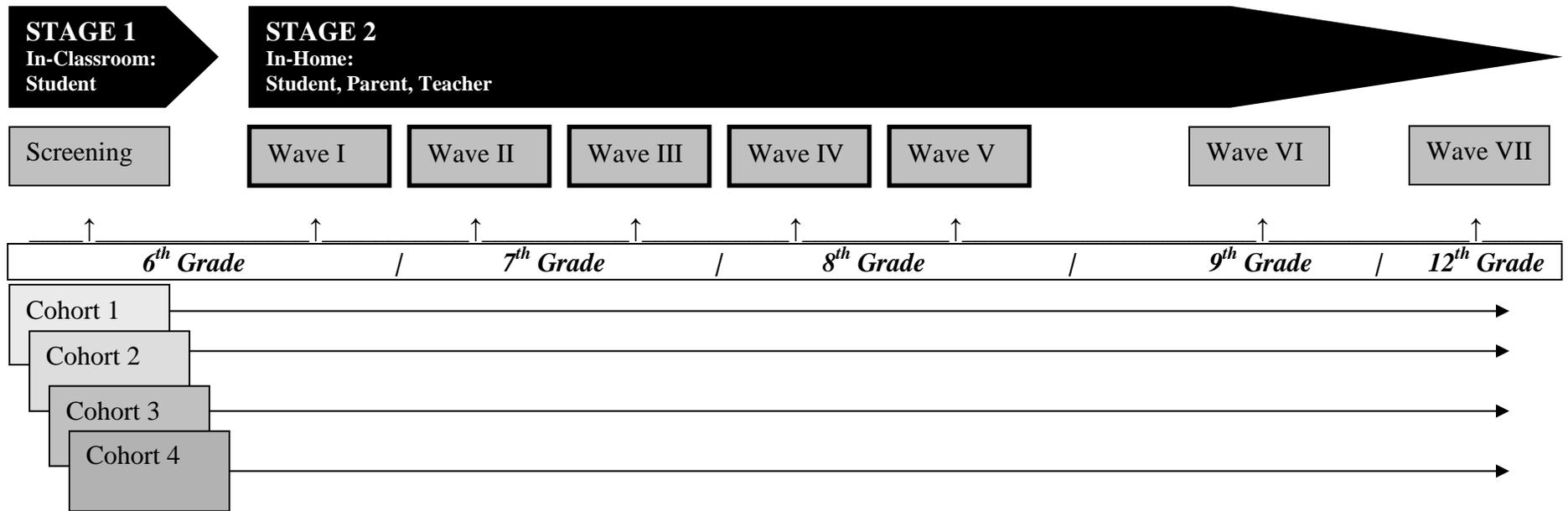


Table 1. Wave 1 Characteristics of the DPP study sample participating in Waves 1, 3 and 5.*

<i>Characteristic</i>	Wave 1 (n=521)		Wave 3 (n=446)		Wave 5 (n=447)	
	n	%*	n	%*	n	%*
Sex						
Male	272	52.2	237	53.1	234	52.4
Female	249	47.8	209	46.9	213	47.7
Race						
Native American	21	4.0	16	3.6	19	4.3
Black	148	28.4	114	25.6	115	25.7
Asian	97	18.6	78	17.5	79	17.7
White	255	48.9	238	53.4	234	52.4
Ethnicity						
Hispanic	53	10.2	46	10.3	48	10.7
Parent Nativity						
Both US-born	352	67.6	312	70.0	313	70.0
At least one foreign-born	162	31.1	133	29.8	131	29.3
<i>missing</i>	7	1.3	1	0.2	3	0.7
Youth Nativity						
US-born	464	89.1	406	91.0	410	91.7
Foreign-born	45	8.6	36	8.1	36	8.1
<i>missing</i>	12	2.3	4	0.9	1	0.2
Household Income						
<\$25,000	139	26.7	106	23.8	105	23.5
\$25,000-\$49,999	121	23.2	103	23.1	105	23.5
\$50,000-\$74,999	99	19.0	82	18.4	83	18.6
\$75,000+	162	31.1	155	34.8	154	34.5
Medicaid Recipient						
Yes	144	27.6	111	24.9	112	25.1
<i>missing</i>	2	0.4	1	0.2	1	0.2

Education of Primary Caregiver							
	Less than high school	38	7.3	28	6.3	25	5.6
	High school diploma/GED	84	16.1	60	13.5	66	14.8
	Some post-secondary	148	28.4	125	28.0	129	28.9
	Bachelor's degree or higher	251	48.2	233	52.2	227	50.8
Adults in Household							
	Two or more	379	72.7	328	73.5	327	73.2
	One	142	27.3	118	26.5	120	26.9
Children (<18 years old) in Household							
	One	127	24.4	109	24.4	109	24.4
	Two	234	44.9	207	46.4	209	46.8
	Three	96	18.4	80	17.9	82	18.3
	Four or more	64	12.3	50	11.2	47	10.5
Residence							
	With family	498	95.6	428	96.0	434	97.1
	Not with family	23	4.4	18	4.0	13	2.9
Whole-life negative events [±]							
	Zero to two	147	28.2	118	26.5	117	26.2
	Three to four	149	28.6	130	29.2	132	29.5
	Five to Six	120	23.0	108	24.2	107	23.9
	Seven or more	104	20.0	90	20.2	91	20.4
	<i>Missing</i>	1	0.2	0	0	0	0
DPP Screening Group							
	Low depression/Low conduct	209	40.1	186	41.7	184	41.2
	Low depression/High conduct	81	15.6	65	14.6	67	15.0
	High depression/Low conduct	107	20.5	94	21.1	94	21.0
	High depression/High conduct	124	23.8	101	22.7	102	22.8

¥ CDISC complete

* Unweighted

± Caregiver report

Table 2. Estimated period prevalence of comorbid and non-comorbid depressive and conduct disorder in middle school overall and by sociodemographic indicators (n=521)

	Neither		DD		CD		DD+CD		F Test (p-value)
	Estimate (%)	95% CI	Estimate (%)	95% CI	Estimate (%)	95% CI	Estimate (%)	95% CI	
Overall	65.4	60.3 - 70.6	10.2	6.6 - 13.9	14.9	11.2 - 18.5	9.5	6.5 - 12.4	
Sex									1.80 (0.146)
Male	59.8	52.5 - 67.0	11.8	6.6 - 17.0	17.8	12.3 - 23.2	10.7	5.9 - 15.5	
Female	71.5	64.3 - 78.7	8.6	3.7 - 13.5	11.8	6.8 - 16.8	8.1	4.8 - 11.5	
Race									2.30 (0.034)
Native American	38.7	12.3 - 65.0	4.7	0.0 - 12.7	27.2	2.7 - 51.7	29.4	0.0 - 60.0	
Black	57.3	47.5 - 67.2	16.1	7.4 - 24.7	14.3	7.7 - 20.9	12.3	6.3 - 18.2	
Asian	77.2	66.7 - 87.8	10.5	2.0 - 19.0	9.0	2.4 - 15.6	3.3	0.0 - 7.1	
White	65.9	59.3 - 72.5	7.2	3.8 - 10.7	17.4	12.1 - 22.7	9.4	5.6 - 13.2	
Ethnicity									2.43 (0.065)
Hispanic	56.4	39.8 - 72.9	5.3	0.0 - 11.7	15.0	4.4 - 25.7	23.3	7.4 - 39.2	
Non-Hispanic	66.4	61.1 - 71.8	10.8	6.9 - 14.7	14.9	11.0 - 18.7	7.9	5.2 - 10.6	
Annual household income									
\$25,000+	69.3	63.7 - 74.8	8.2	5.1 - 11.4	13.9	9.8 - 17.9	8.6	5.2 - 12.0	1.84 (0.139)
<\$25,000	55.1	43.9 - 66.3	15.6	5.8 - 25.5	17.6	9.6 - 25.5	11.7	5.8 - 17.6	
Adults at home									2.66 (0.048)
Two or More	69.2	63.4 - 74.9	9.3	5.4 - 13.2	13.9	9.7 - 18.1	7.6	4.2 - 11.0	
One	54.0	43.4 - 64.5	13.2	4.7 - 21.6	17.8	10.1 - 25.5	15.1	8.7 - 21.5	
Parent nativity									0.71 (0.544)
Both US-Born	62.7	56.7 - 68.8	11.9	7.2 - 16.5	15.7	11.3 - 20.0	9.7	6.3 - 13.1	
At least one foreign-born	70.5	61.6 - 79.3	7.8	2.3 - 13.3	12.9	6.8 - 19.0	8.8	3.5 - 14.2	
Caregiver education									0.73 (0.535)
High school or less	60.4	48.8 - 72.0	14.0	5.2 - 22.8	13.5	5.9 - 21.1	12.1	3.9 - 20.3	
Beyond High school	67.1	61.5 - 72.6	9.0	5.3 - 12.8	15.3	11.1 - 19.5	8.6	5.7 - 11.5	
Negative life events									3.99 (0.008)
Zero to four	69.7	63.3 - 76.0	10.2	5.8 - 14.7	14.7	10.0 - 19.5	5.3	2.4 - 8.3	
Five or more	59.0	50.9 - 67.1	10.3	4.3 - 16.2	15.1	9.6 - 20.5	15.7	9.9 - 21.6	

Table 3. Association between stressful life events (SLEs) and non-comorbid and comorbid depression and conduct disorders during early adolescence (n=521)

			Five or more stressful life events					
	<5 SLEs (%)	5+ SLEs (%)	Unadjusted Model		Model 2*		Model 3 [±]	
			OR	95% CI	OR	95% CI	OR	95% CI
Neither	61.0	39.0	<i>ref</i>		<i>ref</i>		<i>ref</i>	
DD only	56.9	43.1	1.18	0.53, 2.66	1.18	0.52, 2.67	1.05	0.42, 2.58
CD only	56.4	43.6	1.21	0.68, 2.14	1.21	0.68, 2.14	1.10	0.63, 1.90
Comorbid DD/CD	31.0	69.0	3.49	1.69, 7.23	3.49	1.70, 7.18	3.04	1.34, 6.89

* Adjusted for race (Native American, Black, Asian, White)

± Adjusted for number of adults in the home (one vs. two or more)

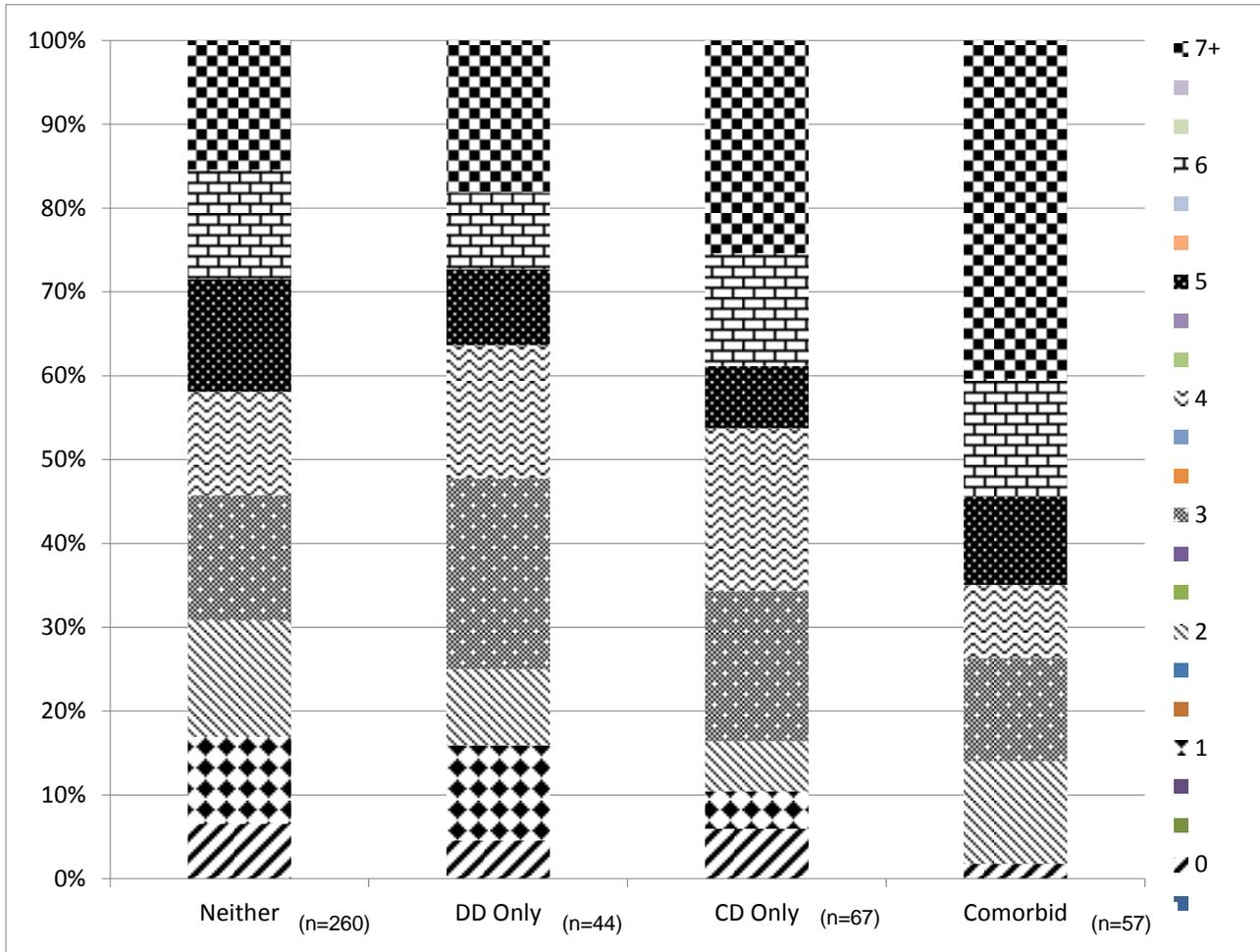
Table 4. Association between stressful life events and comorbid depressive and conduct disorders during early adolescence (n=521).

	Five or more negative life events					
	<u>Unadjusted Model</u>		<u>Model 2*</u>		<u>Model 3[±]</u>	
	OR	95% CI	OR	95% CI	OR	95% CI
Comparison 1						
DD only	ref		ref		ref	
Comorbid DD/CD	2.95	1.06, 8.20	2.94	1.06, 8.20	2.90	0.91, 9.26
Comparison 2						
CD only	ref		ref		ref	
Comorbid DD/CD	2.89	1.21, 6.89	2.88	1.21, 6.85	2.77	1.08, 7.07

* Adjusted for race (Native American, Black, Asian, White)

± Adjusted for number of adults in the home (one vs. two or more)

Figure 2: Frequency of lifetime stressful life events at baseline by middle school cumulative psychopathology group (n=428)*.



*Non-imputed, unweighted data

Table 5. Summary of characteristics that may differentiate adolescents with comorbid depressive and conduct disorders from those with non-comorbid disorders or no disorders				
	DD+CD	DD alone	CD alone	Neither disorder
<i>Sex</i>	~	~	Male	Female
<i>Race</i>	Black, Native American	Black	Native American, White	Asian
<i>Ethnicity</i>	Hispanic	~	~	~
<i>Income</i>	~	Low income	~	~
<i>Adults in home</i>	Single caregiver	Single caregiver	~	~
<i>Parent nativity</i>	~	~	~	At least one foreign-born
<i>Caregiver education</i>	~	High school or less	~	~
<i>Negative life events</i>	High burden	~	~	Low burden

APPENDIX A: DSM-IV Diagnostic Criteria

Major Depressive Disorder

- Five (or more) of nine specific symptoms present throughout the same two-week period:
 - Depressed mood (**Note:** in children and adolescents, can be irritable mood)
 - Marked diminished interest/pleasure
 - Significant weight loss or gain (**Note:** in children, consider failure to make expected weight gains)
 - Insomnia or hypersomnia
 - Psychomotor agitation/retardation
 - Fatigue or loss of energy
 - Feelings of worthlessness
 - Diminished ability to concentrate
 - Recurrent suicidal ideation
- At least one of the symptoms must be either 1) depressed mood or 2) diminished interest/pleasure
- The symptoms must cause significant distress or impairment of functioning in social, occupational, or other important areas
- Depression should not have been precipitated by the direct action of a substance or a general medical condition
- Symptoms should not meet criteria for a mixed episode (i.e., for both manic and depressive episode)
- Symptoms are not better accounted for by bereavement (i.e., the symptoms persist for longer than 2 months or are characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation)
- A major depressive episode should not be superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or a psychotic disorder not otherwise specified (NOS)

Note: For a diagnosis of Minor Depressive Disorder, at least two but fewer than the five items required for diagnosis of Major Depressive Disorder are present. At least one of the symptoms must be either 1) depressed mood or 2) diminished interest/pleasure.

Dysthymic Disorder

- Depressed (or irritable) mood for most of the day for more days than not as indicated by subjective account or observation by others for at least 1 year; in children, the parental report may emphasize behavioral difficulties expressing depression, whereas the child can give a better account of internalizing symptoms, including suicidal ideation
- The presence, while depressed, of two (or more) of the following: (1) poor appetite or overeating, (2) insomnia or hypersomnia, (3) low energy or fatigue, (4) low self-esteem, (5) poor concentration or difficulty making decisions, and (6) feelings of hopelessness

- During the one-year period of the disturbance, the person has never been without the symptoms in criteria A and B for more than 2 months at a time
- No major depressive episode has been present during the first year of the disturbance; that is, the disturbance is not better accounted for by chronic major depressive disorder or major depressive disorder in partial remission
- No manic episode, mixed episode, or hypomanic episode is noted, and criteria have never been met for cyclothymic disorder
- The disturbance does not occur exclusively during the course of a chronic psychotic disorder, such as schizophrenia or delusional disorder
- The symptoms are not due to the direct physiologic effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism)
- The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

Oppositional Defiant Disorder

- A pattern of negativistic, hostile, and defiant behavior lasting at least six months, during which four (or more) of the following are present:
 - Often loses temper
 - Often argues with adults
 - Often actively defies or refuses to comply with adults' requests or rules
 - Often deliberately annoys people
 - Often blames others for his or her mistakes or misbehavior
 - Often touchy or easily annoyed by others
 - Often angry or resentful
 - Often spiteful or vindictive
- The disturbance in behavior causes clinically significant impairment in social, academic or occupational functioning.
- The behaviors do not occur exclusively during the course of a psychotic or mood disorder
- Criteria are not met for conduct disorder, and, if the individual is age 18 years or older, criteria are not met for antisocial personality disorder.

Note: Consider a criterion met only if the behavior occurs more frequently than is typically observed in individuals of comparable age and developmental level.

Conduct Disorder

- A repetitive and persistent pattern of behavior in which the basic rights of others or major age-appropriate societal norms or rules are violated, as manifested by the presence of three (or more) of the following criteria in the past 12 months, with at least one criterion present in the past six months:

- Aggression to people and/or animals
 1. Often bullies, threatens or intimidates others.
 2. Often initiates physical fights.
 3. Has used a weapon that can cause serious physical harm to others (e.g., a bat, brick, broken bottle, knife, gun).
 4. Has been physically cruel to people.
 5. Has been physically cruel to animals.
 6. Has stolen while confronting a victim (e.g., mugging, purse snatching, extortion, armed robbery).
 7. Has forced someone into sexual activity.
- Destruction of property
 1. Has deliberately engaged in fire setting with the intention of causing serious damage.
 2. Has deliberately destroyed others' property (other than by fire setting).
- Deceitfulness or theft
 1. Has broken into someone else's house, building or car.
 2. Often lies to obtain goods or favors or to avoid obligations (i.e., "cons" others).
 3. Has stolen items of nontrivial value without confronting the victim (e.g., shoplifting, but without breaking and entering; forgery).
- Serious violations of rules
 1. Often stays out at night despite parental prohibitions, beginning before age 13 years.
 2. Has run away from home overnight at least twice while living in a parental or parental surrogate home (or once without returning for a lengthy period).
 3. Is often truant from school, beginning before age 13 years.
- The disturbance in behavior causes clinically significant impairment in social, academic or occupational functioning.
- If the individual is age 18 years or older, criteria are not met for antisocial personality disorder.