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Early Pubertal Timing Predicts Onset and Recurrence of Depressive Episodes in Boys and Girls

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Abstract

Background: Recurrent depressive episodes during adolescence result in significant impairment and increased risk for subsequent adverse outcomes throughout the lifespan. Evidence suggests that early pubertal timing predicts the onset of depressive episodes (particularly for girls); however, it is not known if pubertal timing prospectively predicts recurrent depressive episodes in youth.

Methods: At baseline, 603 youth (56% female, at baseline: M_{age} = 12.09, SD = 2.35) reported on their pubertal development. Youth and their parents completed a semi-structured diagnostic interview to assess depressive episodes at baseline, and then evaluated for onset repeatedly every six months for a period of 36 months.

Results: Controlling for past history of depression, Cox proportional hazards models examined whether earlier pubertal timing predicted (1) days to first depressive episode from baseline and (2) days to a second (recurrent) depressive episode from the end of the first episode. Early pubertal timing predicted the onset of the first depressive episode after baseline (b =.19, $Wald$ = 5.36, p =.02, HR = 1.21), as well as a recurrent episode during course of study follow-up episode (b =.32, $Wald$ = 6.16, p =.01, HR = 1.38).

Conclusions: Findings reinforce the importance of considering the impact of early pubertal timing on depression risk. Investigation on how pubertal timing interacts with other risk factors to predict depression recurrence is needed.

Rates of depression rise steeply from childhood into adolescence, especially for girls (e.g., Hankin et al., 2015; Merikangas et al., 2010). Onset of depression before adulthood is associated with greater severity and impairment than adult-onset depression (Zisook et al., 2007) and an earlier age of onset increases the likelihood that an individual will have

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recurrent episodes of depression over his or her lifetime (Pettit et al., 2009). In community samples of adolescents who have experienced an episode of depression, approximately 40% have another depressive episode within three to five years (Lewinsohn, 1994; Rao et al., 1999), and rates of recurrences may be higher in clinical samples of adolescents (Birmaher et al., 1996; Kovacs, 1996).

Recurrent depressive episodes during adolescence results in social, educational, and occupational impairment as well as increased risk for suicide, substance abuse, and other forms of psychopathology (Birmaher et al., 2002; Hammen, Brennan, Keenan-Miller, & Herr, 2008; Wilson et al., 2014). Predicting and preventing the recurrence of depression remains an important clinical challenge (Curry, 2014; Lewinsohn, et al., 1999; Melvin et al., 2014), and there is a need to identify risk factors specifically associated with the recurrence of depression (Burcusa & Iacono, 2007; Lewinsohn et al., 1999; Monroe & Harkness, 2005). However, relatively little is known about the risk factors that prospectively predict recurrent depressive episodes in youth.

In a few studies, parental history of depression (Birmaher et al., 2004; Lewinsohn et al., 2000, Weissman et al., 2000) has been significantly related to initial onset as well as recurrence of depressive episodes in youth. Research has also found that higher levels of negative emotionality, externalizing symptoms and abuse at age 11 resulted in higher risk of depression onset and recurrence of depressive episodes by age 17 (Wilson et al., 2014). However, some factors associated with the first onset of depression in adolescents are not necessarily associated with recurrent episodes of depression during adolescence (Burcusa & Iacono, 2007). For example, SES (i.e., Hollingshead four-factor index) and comorbid diagnoses of psychopathology (e.g., anxiety, behavior disorders) are related to the initial onset of depression during adolescence but neither predicts the likelihood of recurrent episodes of depression (Birmaher et al., 2004; Kovacs, 2001; Lewinsohn et al., 2000). It is important to identify risk factors specifically associated with the recurrence of depression, as they may vary from risk factors related to the initial onset of depression (Burcusa & Iacono, 2007; Lewinsohn et al., 1999).

Is early pubertal timing associated with both the onset and recurrence of depressive episodes?

For both boys and girls, significant evidence supports that early pubertal timing (i.e., maturing physically earlier than peers) is a risk factor for depressive symptoms (e.g., Graber, 2013; Hamlat et al., 2019; Mendle et al., 2012; Ullsperger & Nikolas, 2017). Evidence supports that early pubertal timing predicts the onset of depressive episodes in girls (Copeland et al., 2010; Graber et al., 2004; Graber, 2013). For example, in a female only sample, early maturation predicted depressive episode onset in young adulthood (Copeland et al., 2010). Likewise, Stice, Presnell, & Bearman (2001) found that earlier age at menarche (< 11.6 years) predicted increased risk of a depressive episode over one year. In a sample of adult women, earlier age at menarche was associated with increased risk of a depressive episode during the 12 months prior to assessment (Toffol et al. 2014). Another study found

no association between age of menarche and onset of depressive episodes during the ages of 15 to 30 (Boden, Fergusson, & Horwood, 2011).

It is presently unclear if pubertal timing predicts the onset of depressive episodes in boys, especially as many of the seminal studies of pubertal timing as a risk factor for depression disorders did not include boys. Additionally, foundational work operationalized pubertal timing as age at menarche, or using categorical variables of pubertal timing (which is not current best practice: Senia, Donnellan, & Neppl, 2018; Smith-Woolley, Rimfeld, & Plomin, 2017; Toffol et al. 2014). A small meta-analysis reported that evidence supports early pubertal timing as a risk factor for the onset of depression in girls, but more studies of high quality are needed as the overall quality of the evidence was low (Galvao, et al. 2014).

Some research has emerged to suggest that pubertal timing may serve as a risk factor for depressive disorders in boys as well as girls. For both boys and girls, early pubertal timing was associated with the onset of a depressive disorder two years later (Alloy et al., 2014). Similarly, early maturing boys and girls were more likely to be diagnosed with an internalizing disorder (i.e., major depression, dysthymia, separation anxiety disorder, or general anxiety disorder) (Jin et al., 2008). In contrast, Graber et al. (1997, 2004) found that perceived early maturation in girls, but not boys, was associated with the onset of major depressive disorder (MDD) through age 24. Overall, it has not been established whether early pubertal timing predicts the onset of depression for boys. Early pubertal timing may function as a risk factor for onset of depressive episodes for girls, but not for boys. Moreover, research has yet to determine if pubertal timing prospectively predicts the likelihood of recurrent depressive episodes for boys and girls.

The current study

As predictors of the recurrence of depression in youth are understudied and research suggests that there may be different risk factors for the onset vs. the recurrence of depression, there is a need to clarify whether pubertal timing is a risk factor for both initial and recurrent depressive episodes for boys and girls. The current study evaluated if early pubertal timing prospectively predicts a) the onset of a depressive episode, b) the onset of recurrent (two or more) depressive episodes over time, and c) if results vary by gender. At baseline, youth reported on their pubertal development. At seven follow-up assessments over a three-year longitudinal period (i.e., every six months follow-ups), trained interviewers assessed youth diagnoses of depression by conducting semi-structured interviews with youth and their parents. Assessing depression onset in windows of every 6 months allows for more precise ascertainment of depressive episodes, which is critical to investigating depression recurrence rigorously.

We used survival analyses to examine whether the interaction between pubertal timing and gender prospectively predicted time to first depressive episode after baseline and second depressive episode (from end of first episode) during the 36-month study period. Consistent with prior literature, we expected to find that early maturing girls would demonstrate shorter time to onset of the first post-baseline depressive episode, in comparison to on-time or later maturing peers. We also hypothesized that early maturing girls would demonstrate shorter

time to onset of a second, recurrent episode of depression, than on-time or later maturing peers. Given the lack of definitive evidence regarding the relationship between pubertal timing and the onset and recurrence of depressive episodes in boys, we did not make *a priori* hypotheses for boys.

Method

Participants and procedure

The present study used data from the Gene, Environment, and Mood (GEM) study. Additional study design and sample characteristics are described in Hankin et al., 2015. Youth and their parents were recruited from the general communities in the Denver metropolitan and central New Jersey areas.

Ethical Considerations.—Appropriate informed consent was obtained, and study protocol was approved by IRBs of the University of Denver and Rutgers University.

Brief information letters were sent home directly to families with a child in third, sixth, or ninth grades in the participating school districts. Exclusion criteria included child autism spectrum disorder, psychosis, and the presence of intellectual or developmental disabilities. Of the families to whom letters were sent, 1108 parents responded to the letter and called the laboratory for more information. Of the families who initially contacted the laboratory, 665 (60% participation rate) qualified as study participants. The remaining 460 (41%) were considered nonparticipants: 4 (1%) because the child had an autism spectrum disorder or low IQ; 13 (3%) were non–English-speaking; 330 (71%) declined after learning about the study's requirements; and 113 (25%) were scheduled but did not arrive for assessment. The present study included 603 youth (56% female, at baseline: M_{age} = 12.09, SD = 2.35) with complete data from the baseline assessment (i.e., pubertal development and diagnostic interview) and for whom at least one diagnostic interview follow-up assessment over the 3-year follow-up was available. The racial background of youth was reported as Caucasian (69.0%), African-American (10.5%), Asian or Pacific Islander (9.2%), and American Indian or Alaskan Native (0.8%); 10.5% of participants were of other racial background, and 12.8% of the sample reported their ethnicity as Hispanic.

Youth and their parents visited the laboratory for an initial visit, in which youth provided informed written assent and parents provided informed written consent for their participation. At baseline, youth and their parents completed a semi-structured diagnostic interview (Schedule for Affective Disorders and Schizophrenia for School Age Children [K-SADS-PL]; Kaufman et al., 1997), and youth reported on their pubertal development. After baseline, youth and their parents completed diagnostic interview measures every six months for a period of three years (36 months). There were no significant differences in age, gender, and history of depression at baseline (p > .05) between youth who completed the study through the 36-month assessment (N = 512) and youth who did not complete the study.

Two to three years has been recommended as an appropriate length of time for a sufficient examination of recurrent depressive episodes. The majority of depression recurrences occur within two years from the end of the last episode, and the longer time an individual stays in

remission from depression, the lower the probability is of having another depressive episode (Monroe & Harkness, 2011).

Primary measures

Pubertal Timing.—Pubertal development was assessed with the Pubertal Development Scale (PDS; Petersen, Crockett, Richards, & Boxer, 1988). The PDS is a six-item self-report questionnaire that assesses the current status of pubertal development. Each characteristic (except menstruation, which is coded 1 = *has not begun*, 4 = *has begun*) is rated on a 4-point scale (1 = *no development*, 2 = *development has barely begun*, 3 = *development is definitely underway*, 4 = *development is complete*). The PDS has demonstrated good psychometric properties and convergent validity based on self- and physician-rated Tanner stages (Petersen et al., 1988; Siegel, Yancey, Aneshensel, & Schuler, 1999). Prior to conducting analyses, the PDS total score was regressed on age separately for girls and boys, and the standardized residual obtained was used as the measure of pubertal timing (Dorn et al., 2006; Dorn, Susman, & Ponirakis, 2003; Hamlat et al., 2014). Larger values of the timing variable indicate more advanced pubertal status relative to others of the same age and gender (i.e., earlier pubertal timing). Internal consistency for child report of the PDS at baseline was 0.82 for boys, and 0.83 for girls.

Depression.—Youth depression diagnoses were assessed at each time point by interviewers using the K-SADS-PL (Kaufman et al., 1997), who were trained and supervised by Ph.D.-level licensed clinical psychologists. Interviewers used both child and parent report to establish depressive episodes using best estimate procedures for the K-SADS, in which the interviewer used his or her best judgment to integrate and resolve reports between child and parent report (Klein et al., 2005). Reliability estimates based on 20% of interviews indicated good reliability (κ = .91).

Youth were determined to have experienced a depressive episode if they met Diagnostic and Statistical Manual of Mental Disorders – Fourth Edition (DSM-IV; American Psychiatric Association, 1994) criteria for major depressive disorder (MDD) definite (five threshold depressive symptoms lasting at least 2 weeks), MDD probable (four threshold depressive symptoms lasting at least 2 weeks), or minor depressive disorder (mDD) definite (two or three threshold depressive symptoms lasting at least 2 weeks). To be diagnosed with MDD definite, MDD probable, or mDD definite, an individual must meet for at least one criterial depression symptom, additional symptoms, and demonstrate impairment or clinical distress. In adolescents, MDD probable and mDD definite are associated with significant disease burden, including functional impairment and elevated risk for suicide in adolescents (Avenevoli et al., 2015, Baláz et al., 2013). Past research demonstrates that depression exists on a dimensional continuum (e.g., Hankin et al., 2005), so all three depressive diagnoses were collapsed into a single variable for study analyses.

At baseline, youth and a parent were interviewed to assess the youth's lifetime history of depression. In line with epidemiological samples (e.g., Thapar, et al., 2012), 20% of the sample had experienced a depressive episode before study baseline. Youth history of depression at baseline was dichotomized as 1 = one past depressive episode occurring before

baseline or 0 = no past depressive episode before baseline. At subsequent 6-month follow-ups, youth and a parent were interviewed to ascertain if the child met DSM-IV diagnostic criteria for a depressive episode in the time since the previous K-SADS interview. Depression onset following baseline was categorized as 0 = no episode, 1 = the onset of a single episode, 2 = the onset of recurrent (two or more episodes) during the 36 month period. To minimize the possibility of false positives, each depressive recurrence was defined as a new episode if there was a period of remission of at least two months minimum from the previous episode, which is the standard approach in DSM-IV (American Psychiatric Association, 1994).

Data analytic plan

We conducted two separate survival analyses (Cox proportional hazards models) to examine (1) whether earlier pubertal timing predicts time (in days) to first depressive episode from baseline and (2) whether earlier pubertal timing predicts time to a second, recurrent depressive episode from the end of the first episode. Using survival analyses takes into account participants who had not experienced a depressive episode (or a recurrent episode in the second model) by the end of the study. In both analyses, we examined the interaction of gender with pubertal timing to predict time to first and second onset of depression after baseline. Youth past history of depression (1 = one depressive episode occurring before baseline or 0 = no depressive episode before baseline) was entered as a covariate in all analyses, and sensitivity analyses (i.e., interaction between past depressive status and pubertal timing) were run separately to determine if results differed between youth who had experienced a pre-baseline episode and youth with no history of depression.

Results

Preliminary analyses

Descriptive statistics for the full sample, as well as by gender, are reported in Table 1. At baseline, 121 (20.1%) of the participants had experienced a past depressive episode, and there was no gender difference in the proportion of participants who had a depressive episode before baseline, $\chi 2 = 0.96$ (602), $p = .33$. There was not a significant difference in pubertal timing between those who experienced a depression episode before baseline and those who did not, $t(603) = .06$, $p = .95$. There was a significant gender difference in the onset of depressive episodes after baseline, $\chi 2 = 14.27$ (2), $p = .001$. In the 36 months after baseline, 35 (13.3%) boys and 56 (16.5%) girls experienced the onset of one depressive episode, and 47 (13.8%) girls and 14 (5.3%) boys experienced the onset of recurrent (two or more) depressive episodes. The range of recurrent episodes during the study period was two to four (M= 2.61; SD = 0.76).

Pubertal timing and first depressive onset

Cox proportional hazard regression was used to predict time to first depressive episode after baseline (Table 2, Figure 1). Controlling for past history of depression, earlier pubertal timing predicted fewer days to the first depressive episode during the 36-month study period ($b = .19$, $Wald = 5.36$, $p = .02$, HR = 1.21). To examine potential gender moderation, past history of depression, pubertal timing, and gender were entered on the first step, with the

interaction term (pubertal timing x gender) entered on the second step. The addition of the interaction of pubertal timing and gender was not significant according to traditional conventional criteria (b =.32, *Wald* = 3.10, *p* =.08, HR = 1.37). Sensitivity analyses showed that the relationship between pubertal timing and days to the first depressive episode did not differ for those who had experienced a depressive episode before baseline and for those who had never experienced a depressive episode; the interaction between pubertal timing and past history of depression was not significant (b =−.02, *Wald* = .01, *p* =.92, HR = 0.98). [1]

Pubertal timing and second depressive onset

Next, we used Cox proportional hazard regression to predict days to second depressive episode from the end of the first depressive episode (Table 2, Figure 2). Controlling for past history of depression, earlier pubertal timing predicted fewer days to the recurrent episode (*b* =.32, *Wald* = 6.16, *p* =.01, HR = 1.38). To examine potential gender moderation, past history of depression, pubertal timing, and gender were entered on the first step, with the interaction term (pubertal timing x gender) entered on the second step. The addition of the interaction of pubertal timing and gender was not significant (b =.47, *Wald* = 2.24, *p* =.14, HR = 1.60). The relationship between pubertal timing and days to the recurrent depressive episode did not differ by past history of depression; the interaction between pubertal timing and past history was not significant (b =.07, *Wald* = .09, *p* =.77, HR = 1.08).

Discussion

An abundance of past literature supports earlier pubertal timing as a risk factor for depression in youth, particularly in girls; however, little work has been done to determine the role that pubertal timing plays in depression recurrence. The results of the present longitudinal study suggest that earlier pubertal timing is a prospective risk factor for both onset and recurrence of depressive episodes. After controlling for history of depression, early pubertal timing predicted first depressive episode and fewer days to a recurrent depressive episode (from the end of the first depressive episode) over the 3-year follow-up. Overall, more girls experienced recurrent depressive episodes than boys; gender did not moderate the relationship between pubertal timing and depression onset, in that pubertal timing predicted the occurrence of the first and recurrent depressive episode for both girls and boys. As both early-maturing boys and girls were at higher risk for depressive episodes, the current findings provide some support for the most widely accepted theory for the association between early pubertal timing and psychopathology, maturational disparity (Ge, & Natsuaki, 2009). Maturational disparity posits that children who experience pubertal development before their peers may not have the cognitive or emotional resources to deal with psychosocial consequences (e.g., becoming sexually active) of early pubertal maturation, which may ultimately lead to depression.

Early pubertal timing predicted both the onset of a first episode and recurrent episode of depression during adolescence. Some past studies (e.g., Graber et al., 1997, 2004) have

[1]As a secondary sensitivity analysis, we ran the analyses controlling for age. The effect of pubertal timing on both onset and recurrence were similar with and without age covaried and does not change our overall interpretation of the results. Sensitivity analyses controlling for age are listed in online Table S1.

found early maturation predicted the onset of depressive disorder for girls, but not boys; however, in the current study, gender did not significantly moderate the relationship between pubertal timing and future onset of depressive episodes. There are several reasons why current findings may differ from those of past research. First, research on pubertal timing as a risk for depressive *episodes* in adolescent boys is limited and previous work has been conducted with predominately female samples (Galvao et al. 2014). Second, the three years of follow-up in the current study extended into late adolescence and a longer follow-up into adulthood could help determine if gender differences occur in the relationship between pubertal timing and the development of recurrent depressive episodes during adulthood. Finally, the interactions of gender and pubertal timing on both depression onset (p =.08) and recurrence (p =.14) did not meet traditional significance level (p <.05) to interpret the simple slopes[2]; however, the gender interactions might be significant with a larger sample size that provides additional power. In that case, it is possible that pubertal timing would predict the onset and recurrence of depression for girls (and not boys).

As early intervention leads to better outcomes for adolescents at risk of recurrent episodes, and adolescents who respond well to treatment for depression still often experience later recurrence (Curry et al., 2014), emphasis should be placed on identifying those at risk for recurrent episodes using premorbid risk factors. Early pubertal timing, parental history of depression, child abuse, negative cognitive style, and high levels of negative emotionality and externalizing symptoms at an early age may be used to predict the likelihood of recurrent episodes during adolescence and so aid in the pre-morbid identification of individuals likely to have a chronic course of depression over the lifespan. Early pubertal timing may be part of a constellation of factors that represent a phenotype for depression characterized by a higher probability of recurrence. Depression displays heterogeneity in its course; about 50% of those diagnosed experience only one episode throughout the lifespan, around 35% have recurrent depressive episodes, and the remaining 15% experience an unremitting course of the disorder (Eaton et al., 2008). Examining risk factors for recurrent depression such as pubertal timing may help us identify the subset of individuals who experience recurrent episodes throughout the lifespan. Moreover, research on how pubertal timing interacts with other risk factors to predict depression recurrence is needed.

Strengths of the present study include three years of follow-up assessment with repeated diagnostic evaluations of depression onset every 6-months. Several limitations of the study should be addressed. The first onset of a depressive episode after baseline was the first lifetime depressive episode for 80% of the study sample as 20% had experienced a pre-baseline episode. Sensitivity analyses found that findings did not differ by past history of depression; however, in order to capture the first lifetime onset of depression in an entire sample, future research would benefit from following a study population from early childhood. Additionally, future studies should follow participants for a longer duration into adulthood to assess the long-term effects of pubertal timing on depression recurrence. Copeland et al. (2010) and Graber et al., (2004) both found that early pubertal timing

[2]For onset, the effect of pubertal timing on boys was b = −.03, *Wald* = 0.40, p =.85, HR = 0.97, 95% CI [0.72, 1.30], for girls it was b = .29, *Wald* = 8.22, p =.004, HR = 1.33, 95% CI [1.10, 1.62]. For recurrence, the effect of pubertal timing on boys was b = −.06, *Wald* = 0.04, p =.84, HR = 0.95, 95% CI [0.55, 1.62], and for girls it was b = .41, *Wald* = 7.75, p =.005, HR = 1.51, 95% CI [1.13, 2.02].

predicts the onset of depressive episodes in females through young adulthood (age 21 and 24, respectively). Extending future research into adulthood would allow for a test of the attenuation hypothesis (i.e., after an initial impact during adolescence, the effects of early maturation may ultimately attenuate, Copeland et al, 2010) against the persistence hypothesis (i.e., negative influences of pubertal timing persist into adulthood and do not diminish, Copeland et al, 2010). Moreover, a longer follow-up interval would increase the likelihood that youth with chronic depression that lasts for an extended period of time (e.g., more than one year) would demonstrate recurrence. In previous studies, those with chronic depression sometimes did not achieve remission during the study period (Klein, 2010; Monroe & Harkness, 2011); risk for recurrence appears to be separate from risk for chronic depression and experts consider chronic depression to be a distinct subtype of depression (Hollon et al., 2006; Klein, 2010).

This study adds to the understudied topic of risk factors for recurrent depression in adolescence and affirms the importance of examining pubertal timing as a risk factor for both depressive symptoms and the onset of depressive episodes. The present analysis adds to the body of literature focused on puberty as a period of high risk for depression and suggests that further investigation on how pubertal timing interacts with other risk factors to predict depression recurrence is warranted. Our findings significantly advance the literature on depression recurrence in adolescence and reinforce the importance of considering the impact of early pubertal timing on both girls and boys.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key points:

Recurrent depressive episodes during adolescence result in significant impairment throughout the lifespan.

This study provides the first evidence that early pubertal timing prospectively predicts recurrent depressive episodes for both boys and girls.

Early pubertal timing may be used to identify individuals likely to have a chronic course of depression.

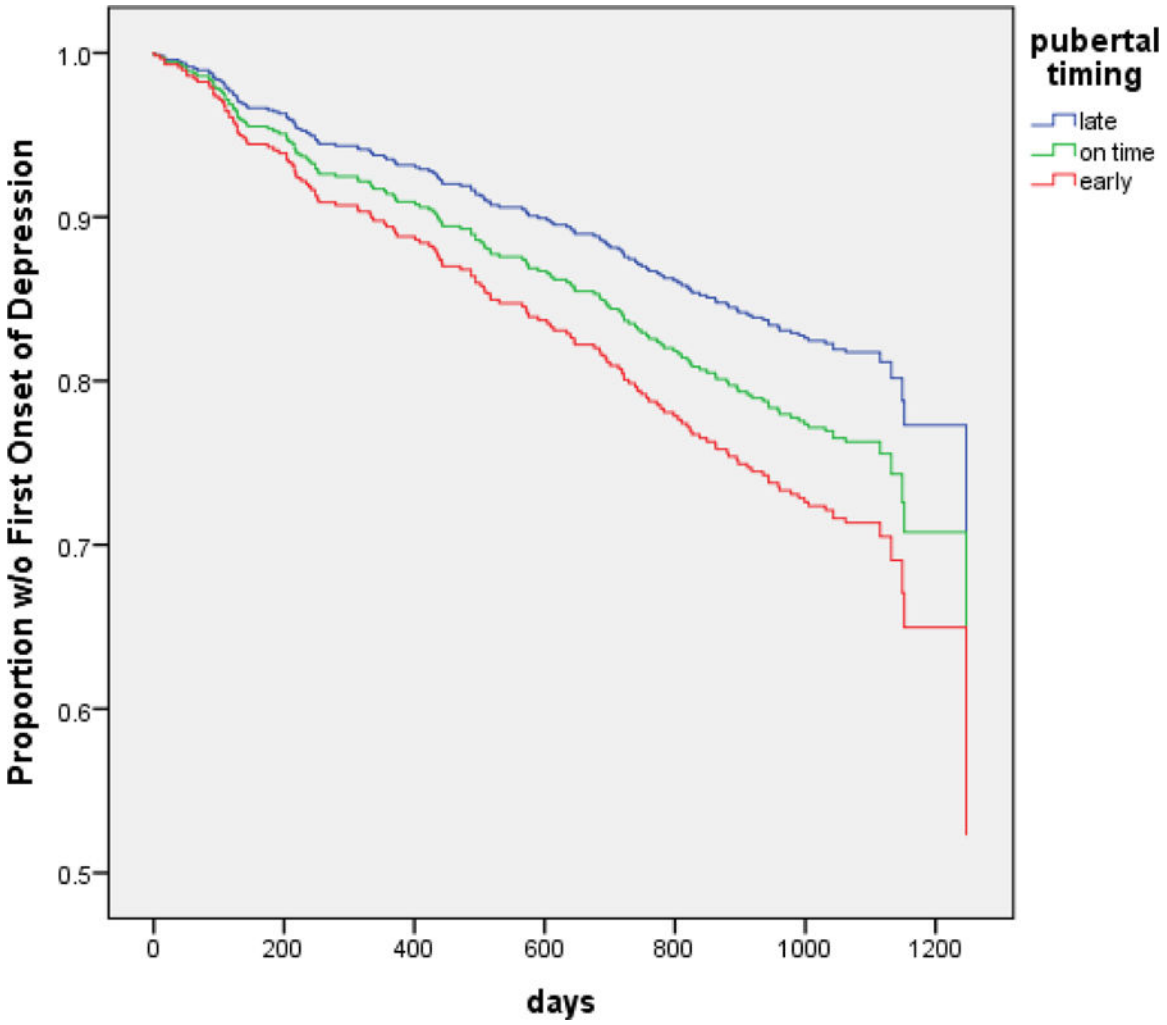

Figure 1.

Survival curves for relationship between pubertal and time until first onset of major depressive episode. Pubertal timing was trichotomized to create early (1 SD above mean), on-time (mean), and late (1 SD below mean).

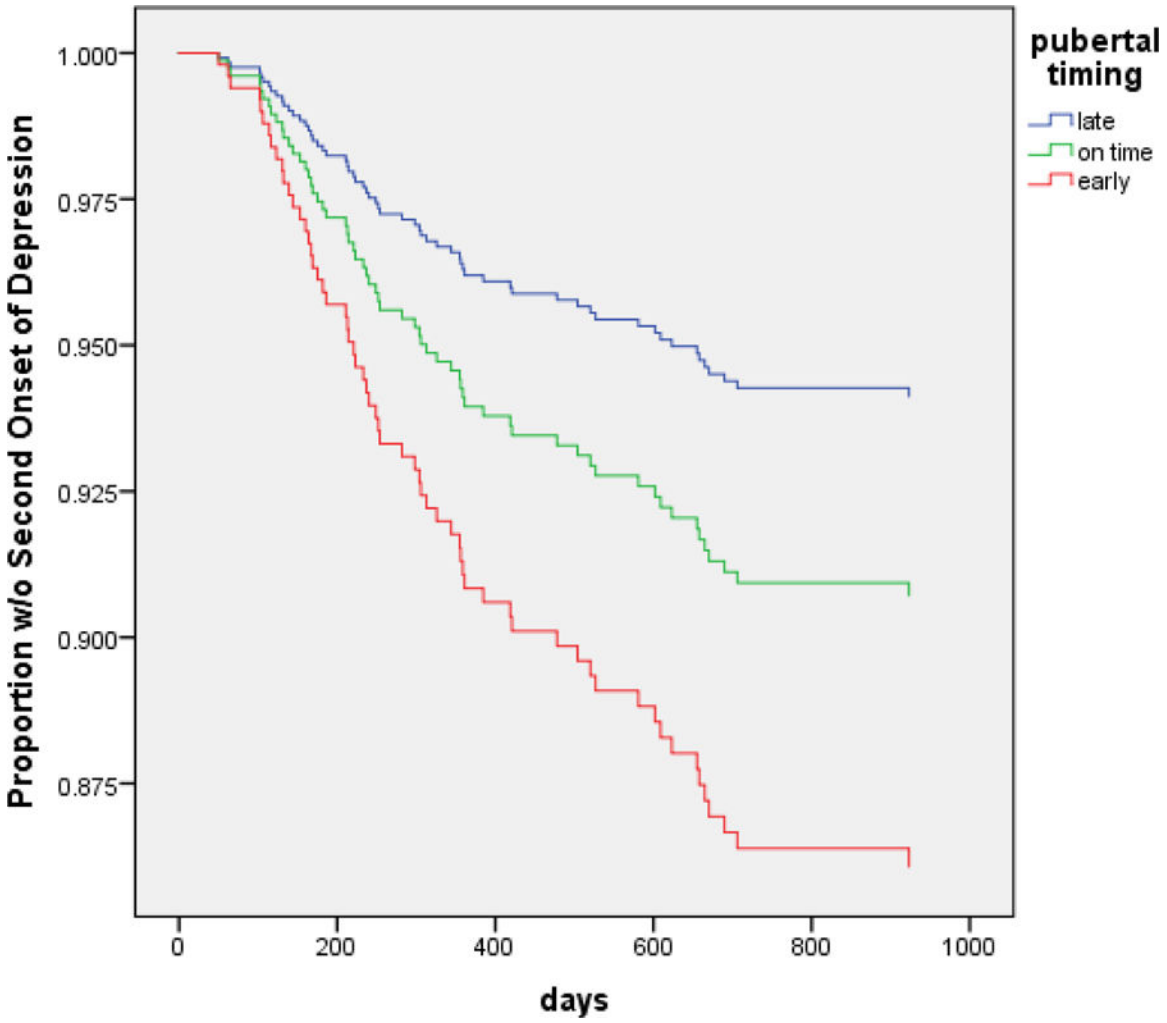

Figure 2.

Survival curves for relationship between pubertal timing and time until second onset of major depressive episode (from end of first episode). Pubertal timing was trichotomized to create early (1 SD above mean), on-time (mean), and late (1 SD below mean).

Table 1

Means and Standard Deviations for Study Variables.

	Past Depressive Episode (at baseline) ***N*** **(%)**	**Prospective Onset of 1 Depressive Episode**[a] ***N*** **(%)**	**Prospective Onset of 2+ Depressive Episodes**[a] ***N*** **(%)**
Full Sample (N = 603)	121 (20.1)	91 (15.1)	61 (10.1)
Girls (N = 340)	73 (21.5)	56 (16.5)	47 (13.8)
Boys (N = 263)	48 (18.3)	35 (13.3)	14 (5.3)
t or $\chi 2$ (*df*)	0.98 (602)	14.27 (2) **[b]	

Note.

* $p < .05$;

** $p \leq .01$;

*** $p \leq .001$.

[a] during the three years after baseline.

[b] whether there is a difference in the distribution of the three categories (no episodes, 1 episode, 2+ episodes)

Table 2

Cox Regression Analysis Evaluating Pubertal Timing as Predictors of the First and Second Depressive Episode During the 36-month Follow-up.

First Depressive Episode						
Predictor	***b***	***SE***	***Wald***	***p***	**HR**	**95% CI**
Past depression at baseline[a]	1.32	.17	59.87	<.001	3.74	[2.68, 5.22]
Pubertal timing at baseline	0.19	.08	5.36	.02	1.21	[1.03, 1.42]
Second Depressive Episode						
Predictor	***b***	***SE***	***Wald***	***p***	**HR**	**95% CI**
Past depression at baseline[a]	1.57	.26	37.47	<.001	4.81	[2.91, 7.96]
Pubertal timing at baseline	0.32	.13	6.16	.01	1.38	[1.07, 1.77]

Note.

[a]reference category is “no past depression”. HR = hazard ratio; 95% CI = 95% confidence interval for the ratio.