PRODROMAL SYMPTOMS OF DEPRESSION: TESTS OF A MODEL OF THE DEVELOPMENT AND REMISSION OF DEPRESSIVE SYMPTOMS

A Dissertation
Submitted to
The Temple University Graduate Board

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in Partial Fulfillment
of the Requirements for the Degree
DOCTOR OF PHILOSOPHY

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by
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August, 2009

ABSTRACT
Prodromal Symptoms of Depression: Tests of a Model of the Development and Remission of Depressive Symptoms
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Doctor of Philosophy
Temple University, 2009
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This study examined the early course of depression by testing a conceptual model for the development and remission of depressive symptoms. In this model, prodromal symptoms emanate from the core pathological processes underlying the disorder and comprise the core syndrome as the earliest symptoms to appear, with episodes of depression representing the more pronounced peaks of symptomatology; the core symptoms would also be the last to remit. Several general hypotheses generated from this model were tested. Additionally, the hopelessness and endogenous subtypes of depression were conceptualized within this model and examined. Cognitive risk for depression and the cognitive personality modes of sociotropy and autonomy were also examined as predictors of specific prodromal and residual symptoms. Correlation and survival analyses were conducted to test the various hypotheses. Results supported the existence of a depressive prodrome as well as the general model being tested. The earliest symptoms to appear in an episode of depression were generally consistent throughout the episode and remained as the last to remit. The order of symptom onset was related to the reverse of the order of symptom remission. The durations for the prodromal and remission phases were significantly correlated. When applied to the hopelessness subtype of depression, and depressions experienced by highly sociotropic individuals, the model held. In the endogenous subtype of depression, and among cognitively high-risk and highly autonomous individuals, the model was not strongly supported.

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CHAPTER 1
INTRODUCTION

The study of prodromal symptoms of illness began in the field of clinical medicine. Relatively recently, the study of prodromes in psychological disorders has been undertaken, primarily in the fields of schizophrenia (e.g., Tully & McGlashen, 2006), panic disorder (e.g., Fava & Mangelli, 1999) and depression (e.g., Fava et al., 1990). The impetus for such investigations stems from the perceived value of a clearer understanding of periods of prodromal symptomatology in these disorders, including the potential utility of prodromal symptoms as early indicators of disorder onset and/or need for treatment. As regards depression, it has been suggested that rapid entry into treatment may increase the effectiveness of the intervention (e.g., Kupfer, Frank, & Perel, 1989), and the amount of time one can be expected to remain in remission after treatment (e.g., Gormley et al., 1999). This stresses the need for early detection of depressive episodes, and highlights the potential utility of recognizing prodromal symptoms as early warning signs of an impending depression, indicating the need for early, and potentially more effective, treatment.

Furthermore, a better understanding of the progression of depressive episodes could aid in the generation of more informed and effective treatment strategies. For instance, the combination and sequence of psychopharmacologic and psychotherapeutic treatment for depression has garnered much attention recently, with the argument being made that a combination of both forms of treatment could yield larger therapeutic gains (see Pampallona et al., 2004 for a review). Recent work has begun to suggest that the particular sequence of treatment modalities can be important for maximizing and maintaining treatment gains, as each may target specific symptoms that the other does not (Petersen, 2006). If individuals (or subgroups of individuals) tend to experience similar prodromal symptoms across episodes, treatment strategies could be tailored to those symptom profiles. An understanding of the

prodromal symptoms experienced would thus inform the process of developing a maximally effective treatment strategy.

The available literature aimed at identifying a discernable prodrome for depressive episodes has generally relied on retrospective reports and relatively small sample sizes. Nonetheless, taken together, the literature involving patterns of early symptom onset indicates that studying the early course of depression holds the potential to inform our understanding of the pathological processes underlying depression and its particular subtypes. However, empirically based, theoretical conceptualizations of the depressive prodrome have not been generated or tested as yet, and are sorely needed.

Background

Several preliminary studies of prodromes in depression have been conducted. Extensive review of the literature yields eight studies on prodromal symptoms in unipolar depression (Fava et al., 1990; Bechdolf et al., 2002; Hopkinson, 1965; Perlis et al., 1997; Cadoret, Widmer & Troughton, 1980; Young & Grabler, 1985; Hays, 1964; Manhert et al., 1997), and another that offers insight into the duration of the prodrome (Winokur, 1976). Among these studies, anxiety/tension, irritability, loss of interest, sleep disturbance, decreased drive or motivation, emotional distance, depressed mood, gastrointestinal problems, fatigue, impaired concentration and decreased energy are reported as prodromal symptoms occurring in a significant proportion of their samples. Additionally, among the studies reporting on the duration of unipolar depressive prodromes, the findings are mixed. The mean prodromal duration ranged from 6 weeks for a sub sample of the participants in the study by Hays (1964) to 23 months (Hopkinson, 1965). Thus, there is a good deal of inconsistency across studies, both in terms of the prodromal symptom profiles experienced and their durations.

The inconsistent findings may be misleading, though. Indeed, some important consistencies have been suggested. In particular, there is evidence of consistency of symptoms

experienced within individuals, across not only episodes of depression, but their prodromes as well. Paykel, Prusoff and Tanner (1976) found similarities between the symptoms experienced during a depressive episode and subsequent relapse following intervening recovery. Young, Fogg, Scheftner and Fawcett (1990) also demonstrated that across recurrent unipolar and bipolar depressive episodes of equal intensity (i.e., similar numbers of symptoms experienced), consistent symptom patterns were observed.

Consistency within individuals across prodromes has been suggested in several preliminary studies of unipolar and bipolar depression. Fava and colleagues (1990), conducting a visual inspection of data from 15 individuals with unipolar depression, noted that the prodromal symptoms of relapse closely resembled those of the preceding initial episode. Molnar, Feeney and Fava (1988) likewise noted the consistency in prodromal symptoms, and the duration of these prodromes, preceding episodes of bipolar depression. Smith and Tarrier (1992) and Keitner and colleagues (1996) also indicated that in studies of bipolar patients, a substantial proportion of patients described a high level of consistency across prodromes. Despite their retrospective nature, and the use of visual inspection of the data as opposed to statistical tests in the studies by Fava and colleagues (1990) and Molnar and colleagues (1988), these studies of successive prodromes and episodes of depression offer preliminary evidence that for a given individual, depressive episodes tend to begin according to consistent symptom sequences, and that the duration of the prodromal period might also be relatively consistent across episodes as well.

Moreover, evidence that the prodromal and residual symptoms of an episode of depression can be quite similar has been offered in different studies. Fava and colleagues (1994) found that, aggregating across a sample of patients treated pharmacologically for depression, the majority (66.7%) of residual symptoms present after treatment were also present in the prodromal phase of the disorder as well. Again, though, visual inspection of the data led to these conclusions, without specifically testing these hypotheses. Similarly, Mahnert and colleagues

(1997) reported that in a sample of 15 individuals treated with SSRI's, tricyclics, or lithium for recurrent unipolar depression, retrospective recall of prodromal and residual symptoms yielded similarity within individuals. The applicability of these findings to our understanding of the relation between prodromal and residual symptoms in depression is tempered by the treatment received in these samples. Still, they highlight the possibility that prodromal and residual symptoms are related.

A relation between prodromal and residual symptoms would be supportive of what has been referred to as the *rollback phenomenon* (Detre & Jarecki, 1971). According to the rollback phenomenon, as depression remits it will repeat, in reverse order, many of the stages and symptoms experienced as the episode developed. Accordingly, the prodromal symptoms of the disorder would be the last symptoms to remit, potentially explaining the relation between prodromal and residual symptomatology. Fava and colleagues (1994) argue that their findings, and those of Manhert and colleagues (1997), provide support for the rollback phenomenon. The rollback phenomenon hypothesis further presupposes a temporal relation between the period of development of the disorder and the duration of the recovery phase, suggesting that the duration of prodromal and residual phases would be similar. Studies of this relation have not been conducted to date.

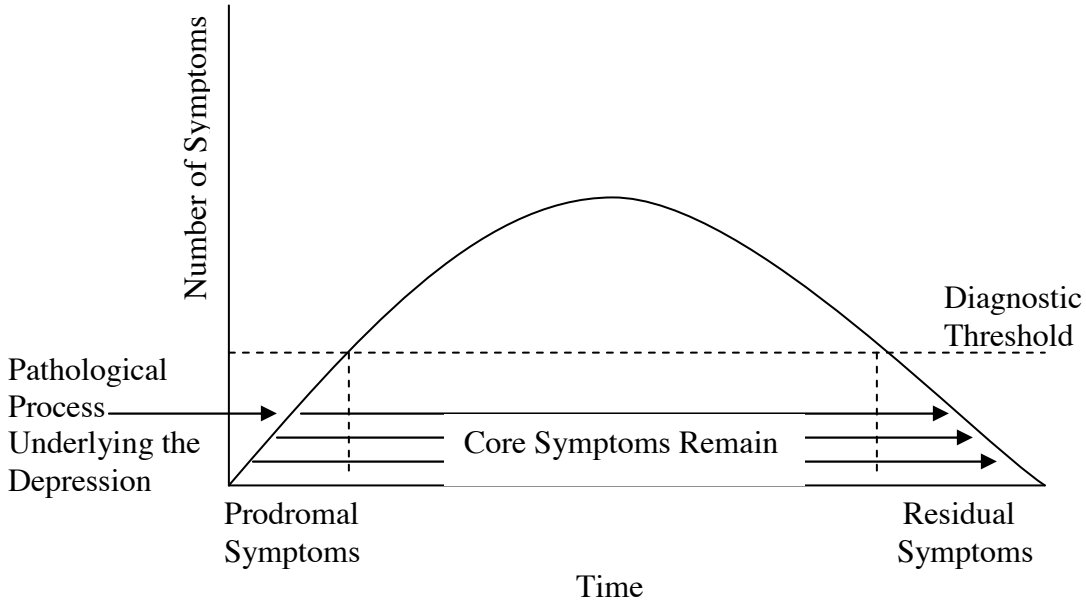
The consistency of symptoms across the prodromal, acute and residual phases of the depressive experience could indicate a consistency of the processes underlying the disorder. This also highlights the importance of identifying and understanding the earliest symptoms in the context of the development of the acute episode. Support for this notion comes from Young and colleagues (1991), who employed survival analyses to demonstrate that the hallmark symptoms of seasonal affective disorder (SAD; hypersomnia, appetite increase, fatigue) were the first symptoms to emerge in a sample of individuals with SAD, with the secondary symptoms emerging afterwards. A conceptualization of the depressive experience derived from such

findings suggests that the mechanisms underlying these symptoms differ, with the earliest symptoms possibly representing a core syndrome, especially if they remain the most stable throughout the depression and persist as residual symptoms. Secondary symptoms "build off of" the core symptoms. This has been hypothesized as a "dual vulnerability" for the development of depressive episodes, including SAD (Young et al., 1991).

Based on the preliminary evidence reviewed above, a conceptual model for the early development and eventual remission of depression can be generated (Figure 1). In this model, the basic pathologic processes leading to symptoms of depression are relatively stable within individuals, and perhaps across individuals experiencing similar subtypes of depression. The core psychopathological processes underlying the disorder and its subtypes are reflected in the prodromal symptoms displayed, which form the core syndrome of the disorder, remain through the depression, and often remain as residual symptoms. Episodes represent the more pronounced peaks of symptomatology.

According to this model, specific subtypes of depression may be expected to display particular prodromal symptoms, reflecting the particular pathological process underlying the disorder subtype. Indeed, Van Praag (1992) suggests that in "5-HT related depression," in which serotonergic function disturbance is hypothesized to be a core pathogenic process in the depression, certain core symptoms deriving from this disturbance (e.g., dysregulation of anxiety and aggression/irritability) will form the core syndrome, whereas the mood disturbance is a subsequent byproduct. Here, it would be expected that anxiety and aggression/irritability would present as the prodromal symptoms. Likewise, the hopelessness theory of depression (Abramson, Metalsky & Alloy, 1989) offers another example. According to this theory, depressogenic inferential styles, in combination with negative life events, will increase the likelihood of

Figure 1. Conceptual Model for the Development and Remission of Depressive Symptoms.



hopelessness, which, in turn, leads to the development of the hopelessness depression (HD) cluster of symptoms (motivational deficit, sad affect, suicidal ideation, low energy, apathy, psychomotor retardation, sleep disturbance, poor concentration and mood-exacerbated negative cognitions). Thus, one would consider hopelessness as a prodromal symptom in HD, expecting it to appear before the onset of the other HD symptoms, which might precede any secondary symptoms.

Like hopelessness depression, endogenous depression, a subtype derived from Klein's (1974) conceptualization, is a widely studied subtype of depression hypothesized to comprise a series of core symptoms. These symptoms of endogenous depression include loss of interest or pleasure, depressed mood, lack of reactivity to environmental changes (mood doesn't lift when something good happens), diurnal variation of mood, feelings of guilt, middle insomnia, early

awakening, psychomotor retardation or agitation, poor appetite, weight loss and suicidal ideation (Klein, 1974; Spitzer, Endicott & Robins, 1978).

Beyond comprising different symptom clusters, the various subtypes of depression may derive from different etiological processes. However, the processes underlying subtypes of depression have largely been unstudied. An exception is hopelessness depression, where it has been demonstrated that a negative cognitive style in interaction with environmental stressors leads to the development of hopelessness and the HD constellation of symptoms and, thus, hopelessness depressions (Alloy et al., 2006). Here, the etiological process is largely a specific cognitive one. Other subtypes of depression, such as the "5-HT related depression" or endogenous depression might be assumed to have different, perhaps more biologically based, etiological processes engendering the depressions. Again, though, no research appears to have been conducted on such hypotheses. The various etiological processes might also predict a variety of courses, responses to treatment, etc., beyond specific symptom constellations.

Sociotropy and autonomy, as cognitive personality dimensions, have also been associated with specific symptoms of depression, based on theory (Beck, 1983) and empirical studies (Robins et al., 1989; 1995; 1997). The depressive symptoms associated with sociotropy include feeling inferior and/or self-conscious, self-blame and/or guilt, crying, restlessness, and nervousness/anxiety. The depressive symptoms associated with autonomy include hopelessness, decreased interest or pleasure in people or activities / anhedonia, irritability, being critical of others, thoughts of death/dying, and suicidal ideation. One might expect, based on the logic of the literature reviewed above, that the core symptoms of depressed individuals who are highly sociotropic or autonomous would appear as the initial symptoms of the disorder. However, no studies of the temporal onset of the depressive symptoms associated with these personality dimensions have been conducted.

Previous studies of prodromes in depression have been beleaguered by methodological limitations. The vast majority of studies have been retrospective, which leads to questionable accuracy of the report, especially considering that prodromal symptoms are often present long before the acute episode is diagnosed or treated, and can be present in a very mild form (Fava & Kellner, 1991). This highlights the importance of employing a prospective assessment of prodromal symptoms that is sensitive enough to capture small changes in the severity of symptoms, as well as one that assesses a broad range of symptoms beyond those that serve as standard diagnostic criteria for a depressive episode. In addition, studies that reportedly support the concept of consistency across prodromes (e.g., Fava et al., 1990; Molnar et al., 1988) and across prodromal and residual symptoms (e.g., Fava, 1994) have used visual inspection of the data, with no specific statistical tests to test these hypotheses. Thus, longitudinal, prospective studies, employing assessments broad enough to cover the range of potential symptoms and sensitive enough to capture minor fluctuations in their intensity (i.e., the presence of prodromal symptoms), are lacking and are necessary to study the conceptual model outlined above.

The Current Study

The purpose of this study was to enhance our understanding of the early course of depression by testing a conceptual model for the development and remission of depressive symptoms (see Figure 1). In this model, prodromal symptoms emanate from the core pathological processes underlying the disorder and comprise the core syndrome as the earliest symptoms to appear, with episodes of depression representing the more pronounced peaks of symptomatology; the core symptoms also would be the last to remit. Several general hypotheses generated from this model were tested.

Additionally, the hopelessness and endogenous subtypes of depression were conceptualized within this model and examined. Exploration of whether the symptomatic

courses of these subtypes differ would build on the theory that the etiological processes underlying the various subtypes are different. Accordingly, application of the conceptual model to these subtypes would allow for tests of the hypothesis that an underlying etiological process will be illuminated in the earliest symptoms that appear and latest symptoms to remit.

The cognitive personality modes of sociotropy and autonomy were also examined as predictors of specific prodromal and residual symptoms, following the evidence that personality can influence the course of depression including the presentation of specific symptom profiles. The aim was to test whether these factors play a role in the etiological process, whereby they generate specific prodromal symptoms that appear to constitute the core syndrome and remain as the latest symptoms to remit.

Hypotheses

General Hypotheses:

1) Individuals will display similar prodromal and residual symptom profiles for a given episode of depression.
2) Individuals will display similar durations of the period of prodromal and residual symptomatology for a given episode.
3) According to the rollback phenomenon, the sequence of prodromal symptom presentation will appear, in reverse, as the symptoms of depression remit.
4) Prodromal symptom profiles will be similar across successive prodromes of successive episodes.

Applied to specific subtypes of depression, the following hypotheses can be generated:

For Individuals Experiencing Hopelessness Depressions:

5) Hopelessness will be the first prodromal symptom experienced among those experiencing a hopelessness depression.

6) The other HD symptoms (sadness, retarded initiation of voluntary responses, suicidality, sleep disturbance (initial insomnia), low energy, self-blame, difficulty in concentration, psychomotor retardation, brooding/worrying, lowered self-esteem, and dependency) will be next to appear, before any other secondary symptoms.
7) As a hopelessness depression remits, it will recapitulate the symptoms presented in the initial stage(s), with the HD symptoms, followed by hopelessness, being the last (potentially residual) symptoms to remit.

For Individuals Experiencing Endogenous Depressions:

8) Loss of interest or pleasure, depressed mood, feelings of guilt, middle insomnia, early awakening, psychomotor retardation or agitation, poor appetite, weight loss and suicidal ideation will be the first prodromal symptoms experienced among those experiencing an endogenous depression.
9) As an endogenous depression remits, it will recapitulate the symptoms presented in the initial stage(s), with loss of interest or pleasure, depressed mood, feelings of guilt, middle insomnia, early awakening, psychomotor retardation or agitation, poor appetite, weight loss and suicidal ideation being the last (potentially residual) symptoms to remit.

For Individuals Demonstrating High Sociotropy:

10) Individuals exhibiting high levels of sociotropy will be more likely to demonstrate the following prodromal symptoms when becoming depressed than individuals with low sociotropy: decreased self-esteem, self-blame and/or guilt, crying, restlessness (psychomotor agitation), and nervousness/anxiety.

11) Among individuals with high levels of sociotropy as compared to low levels, as their depressions remit, the following symptoms will be the last (potentially residual) symptoms to remain: decreased self-esteem, self-blame and/or guilt, crying, restlessness (psychomotor agitation), and nervousness/anxiety.

For Individuals Demonstrating High Autonomy:

12) Individuals exhibiting high levels of autonomy will be more likely to demonstrate the following prodromal symptoms when becoming depressed than individuals with low autonomy: hopelessness, decreased interest or pleasure in people or activities/anhedonia, irritability, and suicidality.

13) Among individuals with high levels of autonomy as compared to low levels, as their depressions remit, the following symptoms will be the last (potentially residual) symptoms to remain: hopelessness, decreased interest or pleasure in people or activities/anhedonia, irritability, and suicidality.

CHAPTER 2
METHODS

This study utilized data collected through the Temple-Wisconsin Cognitive Vulnerability to Depression (CVD) Project (Alloy & Abramson, 1999). This was a two-site prospective examination of the role of cognitive and psychosocial factors in the development of depressive disorders among college students at high and low cognitive risk for depression.

Participants

A two-phase screening process was utilized to select participants for the CVD project at Temple University (TU) and the University of Wisconsin (UW). Phase I assessed cognitive style using the Cognitive Style Questionnaire (CSQ; Alloy et al., 2000) and the Dysfunctional Attitudes Scale (DAS; Weissman & Beck, 1978). A total of 5,378 freshmen (2,438 at TU and 2,940 at UW) completed Phase I. Participants scoring in the highest and lowest quartiles on *both* the CSQ composite for negative events and the DAS were considered the high-risk (HR; N=619: 261 at TU and 358 at UW) and low-risk (LR; N=585: 234 at TU and 351 at UW) groups, respectively. A random subset of participants under the age of 30 in the HR group (N= 313: 167 at TU and 146 at UW) and LR group (N= 236: 130 at TU and 106 at UW) was invited to participate in Phase II of the screening process.

Phase II consisted of administration of an expanded version of the Schedule for Affective Disorders and Schizophrenia-Lifetime diagnostic interview (SADS-L; Endicott & Spitzer, 1978). Both the Diagnostic and Statistical Manual of Mental Disorders, Third Edition-Revised (DSM-III-R; American Psychiatric Association, 1987) and the Research Diagnostic Criteria (RDC; Spitzer, Endicott, & Robbins, 1978) were utilized in assigning diagnoses. In administering the SADS-L and assigning diagnoses to participants, interviewers were blind to risk-group status. Exclusion criteria for the sample included: a current diagnosis of any psychiatric disorder at the time of screening; a history of mania, hypomania or cyclothymia; current psychotic symptoms;

and any serious medical illness at the time of screening that might preclude participation in the longitudinal study. After excluding participants on the basis of these criteria, 209 eligible HR (114 at TU and 95 at UW) and 207 eligible LR (110 at TU and 97 at UW) participants were invited to participate in the study. Of these, 173 HR (83 at TU and 90 at UW) and 176 LR (87 at TU and 89 at UW) participants enrolled in the study. The Time 1 assessment included the Sociotropy-Autonomy Scale (SAS; Beck, Epstein, Harrison & Emery, 1983), among other measures.

This sample of college freshmen was chosen for several reasons. First, the prevalence and severity of depressive disorders may be particularly high during late adolescence (Lewinsohn, Duncan, Stanton & Hautzinger, 1986; Burke, Burke, Reiger & Rae, 1990). This would suggest that a college freshmen sample might be specifically likely to exhibit mood disorders, especially those that are cognitively vulnerable. An additional reason was that this sample was relatively young, and a subset was expected to experience an episode of mood disorder for the first time during this period- a valuable possibility for the purposes of this study. Finally, the practicality of a college freshmen sample is another advantage. Given the longitudinal nature of this study, it would be difficult to obtain a 5-year commitment from participants drawn from the community at large or other non-clinical samples. College students, on the other hand, are readily available and often willing to participate in projects of this sort when adequately compensated.

The current investigation was based on 160 participants (96 HR and 64 LR) from this sample who experienced at least one depressive episode (DSM-IV major depressive episode, RDC major depression episode "definite" and "probable" and RDC minor depression episode "definite") during the first 2.5 years of their participation in the CVD project. Although some participants in this sample did have a history of prior depression before entering the study, a minimum 2-month remission was required to be included in the study. For those participants who

did have a past episode of depression before entering the CVD project, an average of 2.31 (SD= 2.44) years had elapsed since the prior episode.

Measures

The Schedule for Affective Disorders and Schizophrenia- Lifetime version (SADS-L; Endicott & Spitzer, 1978) is a widely used structured diagnostic interview that assesses current and past psychopathology according to the Research Diagnostic Criteria. The SADS-L was used in this study as part of the phase II screening procedure (described above). The SADS has demonstrated high inter-rater reliability across interview sessions and high test-retest reliability (Endicott & Spitzer, 1978).

For the purposes of the CVD project, the SADS was modified and expanded in several ways (Alloy & Abramson, 1999). First, additional questions were included to allow DSM-III-R diagnoses to be made. Second, a more precise set of initial "probes" was included to assess the persistence of depressed mood. Third, components of the Anxiety Disorders Interview Schedule (ADIS; DiNardo et al., 1985) were included in the anxiety section of the SADS. Fourth, some reorganization of the items was conducted such that all items relevant to a particular disorder, both past and current, were presented together. Last, questions were included to assess two cognitive subtypes of depression according to the hopelessness theory (Abramson, Metalsky, & Alloy, 1989) and Beck's (1967) theory.

The expanded version of the SADS-L, like the original version, has demonstrated high levels of inter-rater reliability, with kappas for all diagnoses ≥ .90 (Alloy et al., 2000). As regards validity, HR participants in the CVD project were found to have significantly greater lifetime prevalence and prospective incidence and recurrence of DSM-III-R, DSM-IV, and RDC major depression and RDC minor depression as assessed by the Mod-SADS-L than LR participants (Alloy et al., 2000; 2006).

To assess change in depression over the course of the study, the onset or offset of an episode and for tracking symptoms, an expanded SADS-Change (SADS-C) interview was conducted. The SADS-L and SADS-C differ in that the "L" version was administered to assess current and past depressive experiences, whereas the "C" version was given every 6 weeks throughout the course of the first 2.5 years of follow-up to assess symptoms and episodes of depression during the prospective phase of the study. When an item was endorsed on the SADS-C, several examples were required before a positive rating was made, and strict dating of symptoms (onset and offset) was recorded.

The expanded SADS-C is particularly well suited to assess prodromal and residual symptomatology. The measure assesses a broad range of potential depressive symptoms, beyond those specifically required as standard diagnostic criteria for a depressive episode. Moreover, given its nature as a structured interview administered by trained interviewers, and affording a 6-point severity scale for most items, the SADS-C is sensitive to the onset/offset of symptoms, as well as minor fluctuations in their severity. A broad, yet sensitive assessment is required when investigating prodromal and residual symptoms, as the severity of such symptoms in often milder than that of the symptoms of the acute episode (e.g., Fava & Kellner, 1991). For the current study, the onset, severity and duration of depressive symptoms, as well as the onset and offset of DSM-IV and RDC major and RDC minor depressive episodes, were obtained from this interview.

In the CVD project, inter-rater reliability of the modified SADS-C was high (kappas $\geq$ .90) for all diagnoses (Abramson et al., 1998; Alloy et al., 2006). Test-retest reliability, in which two interviewers blindly interviewed the same participant within two days of each other, obtained kappas $\geq$ .90 for all diagnoses as well (Abramson et al., 1998; Alloy et al., 2006).

For the current study, the following 29 SADS-L and SADS-C depressive symptoms were included in the analyses: sad mood, decreased appetite, weight loss, increased appetite, weight gain, initial insomnia, middle insomnia, early waking, hypersomnia, decreased energy, decreased

interest or pleasure, self blame, difficulty concentrating, indecision, suicidal ideation, psychomotor agitation, psychomotor retardation, crying more, inability to cry, hopelessness, brooding/worry, decreased self-esteem, irritability, dependency, self-pity, somatic complaints, decreased effectiveness, helplessness, and decreased initiation of voluntary responses.

The Cognitive Style Questionnaire (CSQ; Alloy et al., 2000) was developed from the original and revised versions of the Attributional Style Questionnaire (ASQ; Seligman, Abramson, Semmel, & von Baeyer, 1979; Peterson & Villanova, 1988) to assess depressogenic inferences for positive and negative events, although only the composite score for negative events was used in the CVD project. The CSQ consists of 24 hypothetical situations representing equal numbers of positive and negative, interpersonal and achievement events. In the ASQ, participants are asked to identify the cause of an event, to assess its degree of importance and to make attributions as to the internality, stability and globality of the cause using a 1-7 rating scale. In creating the CSQ, Alloy and colleagues (2000) added inferences concerning characteristics about the self and event consequences and adapted the hypothetical situations to better suit a college population. Examples of the negative hypothetical situations from the CSQ include "You take an exam and receive a low grade on it" and "You go to a party with some friends and throughout the whole party people don't act interested in you." The CSQ composite for negative events consists of the total stability, globality, consequences and self-ratings for the 12 negative hypothetical events.

Within the CVD project, internal consistency of the CSQ is good for both negative and positive events (alphas= .88 and .86, respectively; Alloy et al., 2000). The 1-year test-retest reliability is also good (r= .80 for both negative and positive events; Alloy et al., 2000). With respect to validity, Abramson, Alloy and colleagues (Abramson et al., 1998; Alloy et al., 2000; 2006) have shown that the CSQ in combination with the Dysfunctional Attitudes Scale significantly predicts depressive episodes and suicidality in college students.

The Dysfunctional Attitudes Scale (DAS; Weissman & Beck, 1978) is a 40-item self-report questionnaire measuring depressogenic attitudes on a 7-point scale that ranges from "totally agree" to "totally disagree." The DAS assesses perfectionistic expectations of performance, concerns about disapproval, pessimism and causal attributions. In the CVD project, 24 additional achievement- and interpersonally-oriented items were included. Examples of items on the DAS include "I can be happy if I'm not popular at all" and "If I do poorly in school or work, other people will think I'm dumb."

For the DAS, high internal consistency was demonstrated in a college population (alpha= .93; Weissman & Beck, 1978) as well as in an unselected adult population (alpha= .85; Oliver & Baumgart, 1985). In the CVD project, test-retest reliability for 1-year is good (r= .79; Alloy et al., 2000). As regards validity, Weissman and Beck (1978) found the correlation of the DAS with the BDI to range from .48 to .55 in a college sample. Dysfunctional attitudes as measured by the DAS have also been shown to differentiate a group of patients who were depressed from a non-depressed, mixed psychiatric or a non-depressed, normal control group (Hamilton & Abramson, 1983). Finally, risk group status in the CVD project, based on the CSQ and DAS, predicted lifetime history and prospective incidence of depressive disorders (Alloy et al., 2000; 2006).

The Sociotropy-Autonomy Scale (SAS; Beck, Epstein, Harrison & Emery, 1983) is a 60-item questionnaire comprising two 30-item scales. The sociotropy scale contains subscales assessing concerns about the disapproval of others, separation, and pleasing others, and the autonomy scale contains subscales assessing individualistic/autonomous achievement, mobility/freedom from control by others, and preference for solitude. Items are rated on a 5-point scale corresponding to degrees of agreement (0, 25, 50, 75, and 100%). Examples of items include: "I am afraid of hurting other people's feelings" (sociotropy) and "It is very important that I feel free to get up and go wherever I want" (autonomy). The 30-item sociotropy and autonomy total scales have high internal reliability as indicated by coefficient α's of .90 and .83,

respectively (Beck et al., 1983). For the current sample, $\alpha = .937$ for sociotropy and $\alpha = .727$ for autonomy. As regards validity, Bieling, Beck and Brown (2000) conducted factor analyses of the sociotropy and autonomy scales which demonstrated that they each comprise two distinct factors, (sociotropy: Fear of Criticism and Rejection, Preference for Affiliation; autonomy: Independent Goal Attainment, Sensitivity to Others' Control). Each factor is congruent with the theoretical construct of sociotropy or autonomy under which it is subsumed. Moreover, the validity of the SAS sociotropy scale has been demonstrated elsewhere (Clark and Beck, 1991) but the validity of the autonomy scale has not consistently been demonstrated.

Procedures

Participants in the CVD project provided informed consent, which stated that as a participant, $20 would be paid for the Phase II screening and if invited to return, a possible $400-$500 would be paid throughout the duration of the study. Participants were informed that the goal of the study was to gain a better understanding of what contributed to successful and unsuccessful coping with stress during college. Participants were randomly assigned to interviewers after the Phase II assessment using the SADS-L, completed the SAS (among other measures) at the Time 1 assessment, and then participants were interviewed every 6 weeks for the first 2.5 years of the study and every 4 months for the remaining 3 years, for which they were paid $30-$50. Each of these subsequent interviews included the SADS-C, among other assessments. Interviews were conducted in person, when possible; otherwise, interviews were conducted via telephone. Interviews were tape-recorded, providing an opportunity for independent tape reviews by other interviewers. This allowed for the assessment of interrater reliability.

Diagnostic Criteria

The DSM-IV criteria for a major depressive episode include: depressed mood or loss of interest for at least two weeks, 6/7 days per week (12 days minimum) for at least 90% of each

depressed day; and at least 4 other symptoms rated as "clinically significant" (SADS score of 3 or higher) for at least two weeks, overlapping at least 12 days with the criterion A symptom (sad mood or loss of interest). Possible symptoms include: appetite/weight disturbance, sleep disturbance, loss of physical energy, loss of interest or pleasure, guilt, self-blame, concentration difficulties, indecision, suicidal ideation, psychomotor disturbances.

The RDC criteria for a "probable" major depression episode consist of: depressed mood or loss of interest for 6 days minimum for at least 75% of each depressed day; and at least 4 other symptoms rated as "clinically significant" (SADS score of 3 or higher) for at least one week, overlapping 6/7 days with the criterion A symptom (sad mood or loss of interest). Possible symptoms include: appetite/weight disturbance, sleep disturbance, loss of physical energy, loss of interest or pleasure, guilt, self-blame, concentration difficulties, indecision, suicidal ideation, psychomotor disturbances. At least one indicator of impairment is also required for the RDC diagnosis, from among: sought help for the depression, took medication, acted differently because of the depression, depression interfering with social or occupational functioning or ability to get things done.

The RDC criteria for a "definite" major depression episode consist of: depressed mood or loss of interest for at least two weeks, 6/7 days per week (12 days minimum) for at least 90% of each depressed day; and at least 5 other symptoms rated as "clinically significant" (SADS score of 3 or higher) for at least two weeks, overlapping at least 12 days with the criterion A symptom (sad mood or loss of interest). At least one indicator of impairment is also required for the RDC "definite" major episode diagnosis.

The RDC criteria for a "definite" minor depression episode consist of: depressed mood or loss of interest for at least two weeks, 6/7 days per week (12 days minimum) for at least 90% of each depressed day; and at least 2 other symptoms rated as "clinically significant" (SADS score of 3 or higher) for at least two weeks, overlapping at least 12 days with the criterion A symptom (sad

mood or loss of interest). Possible symptoms include: appetite/weight disturbance, sleep disturbance, loss of physical energy, loss of interest or pleasure, guilt, self-blame, concentration difficulties, indecision, suicidal ideation, psychomotor disturbances, crying more or inability to cry, pessimism/hopelessness, worrying/brooding, decreased self-esteem, irritability, dependency, self-pity or excessive somatic concerns. At least one indicator of impairment is also required for the RDC "definite" major episode diagnosis.

Data Analytic Strategy

For the current study, SADS-C data from the CVD project was utilized to ascertain the presence and onset and offset dates of depressive symptoms experienced in relation to a depressive episode. Toward this end, for every participant experiencing at least one DSM-IV and/or RDC major or RDC minor depressive episode, symptoms rated as "slight" (SADS-C rating of 2) or "clinically significant" (SADS-C rating of 3 or higher) throughout each episode were catalogued, recording their onset and offset dates. Symptomatology was traced back from the onset date of the diagnosed episode to the first onset of a depressive symptom before the episode, recording the onset dates of the prodromal symptoms experienced. This period of time, from the appearance of the first depressive symptom rated as slight or clinically significant to the onset date of the acute episode, was defined as the prodromal period. Cataloguing symptoms in this manner provided a qualitative record of the prodromal symptoms experienced. Further, the onset (and, where applicable, offset) dates of the prodromal symptoms experienced provided a measure of the duration of the prodromal period. Similarly, the offset of symptoms continuing past the period of a diagnosable episode of depression was collected to compile a residual symptoms profile and duration.

All depressive episodes were assessed for whether they met criteria for the hopelessness (Abramson, Metalsky & Alloy, 1989) and endogenous (Klein, 1974) subtypes. Episodes could meet criteria for neither, either, or both of these subtypes, and were included in analyses for each

of the subtypes for which they met criteria. It is noteworthy that an episode of depression can simultaneously meet criteria for different subtypes of depression, and as such, the analyses for hopelessness depression and endogenous depression, as well as for individuals with high compared to low levels of sociotropy and autonomy (below), were conducted separately. Doing so allows for the observation that a certain subtype demonstrates a pattern of symptom onset or offset, while another does not, which would be valuable information for assessing the validity of depression subtypes.

Diagnoses of "probable" hopelessness depression were used in the current study, based on the criteria set by Alloy and colleagues (2006, appendix) for the CVD project. These criteria include: (a) hopelessness present for at least 1 week, for 6 out of 7 days of each week; (b) at least 4 criterion symptoms present, overlapping 6 out of 7 days of each week for at least 1 week. The criterion symptoms of hopelessness depression are sadness, retarded initiation of voluntary responses, suicidal ideation, sleep disturbance (initial insomnia), low energy, self-blame, difficulty in concentration, psychomotor retardation, brooding/worrying, lowered self-esteem, and dependency. Diagnoses of endogenous depression were based on RDC criteria for endogenous depression (Spitzer, Endicott & Robins, 1978), adapted to the SADS-C being used in this study: at least 1 criterion A symptom (sad mood, decreased interest or pleasure, lack of reactivity, diurnal variation in mood or a hollow/numb quality to the mood), and at least 4 total symptoms from criterion A and B (decreased appetite, weight loss, middle insomnia, early awakening, self-blame, psychomotor agitation or psychomotor retardation) for at least 1 week.

Preliminary Analyses.

To support the existence and relevance of the prodromal phase of a depressive episode, the number of SADS-C symptoms present immediately before and leading into the acute phase of a depressive episode was compared to the number of SADS-C symptoms present for similar periods of time for non-depressed CVD participants. Toward that end, 60 participants from the

final sample were matched with participants from the CVD Project that did not experience an episode of depression, on the basis of age, gender, ethnicity and cognitive risk status. The period of time before each acute episode of depression, during which at least 1 symptom was continuously present (considered the prodromal phase), was assessed for the number of SADS-C symptoms rated as "slight" (2) or "clinically significant" (3). This was compared to the number of slight or clinically significant SADS-C symptoms present during the corresponding period of time for the matched participant without an episode, with the hypothesis being that individuals who go on to experience an episode of depression will exhibit significantly more symptoms during this period, suggesting a prodromal phase of illness. Further, χ^2 analyses were conducted on the presence of each of the SADS-C symptoms during this period between depressed and non-depressed participants, to assess whether there were specific symptoms that appeared during the prodromal phase across individuals.

To test the specific hypotheses proposed in this study, the following strategies and procedures were utilized:

Hypothesis 1: Individuals will display similar prodromal and residual symptom profiles for a given episode of depression.

To test this hypothesis, the prodromal and residual symptom profiles for each individual in the study, for each episode of depression experienced, were compared using correlation analyses. Such an analytic strategy has been employed previously in studies of the concordance of symptoms present during episodes of depression (e.g., Young et al., 1990). Specifically, to assess the concordance of prodromal and residual symptom occurrence for a given episode, the presence of prodromal and/or residual symptoms rated as "slight" or "clinically significant" on the SADS-C was coded for each period. Cohen's kappa (κ; Cohen, 1960), a measure of homogeneity or agreement across rating periods which adjusts for the magnitude of agreement expected by chance, was calculated based on the presence or absence of the 29 SADS-C

depression symptoms in each episode's prodromal and residual phases. This yielded a measure of symptom agreement for each pair of prodromal and residual phases. A median and mean sample κ was then calculated based on these κ's for each individual episode. As per Landis and Koch (1977), $\kappa < 0.00$ is considered poor agreement or concordance, 0.00-0.20 slight, 0.21-0.40 fair, 0.41 to 0.60 moderate, 0.61 to 0.79 substantial, and 0.80 and above outstanding.

The three assumptions that warrant attention when using this measure are 1) the units of analysis must be independent; 2) the categories of the nominal scale must be independent, mutually exclusive, and exhaustive; and 3) the raters are operating independently. Assumption 1 is assumed to be true in this study, as the units of analysis refer to the individual symptoms coded on the SADS-C. The SADS-C is presumed to be a relatively exhaustive account of potential depressive symptoms, which, although there may be some correlation between certain symptoms, are not considered dependent on one another. Assumption 2 refers to the levels of coding for the symptoms on the SADS-C. Indeed, the coding used for the present analyses categorizes symptoms into "absent," "present to a slight degree," and "clinically significant." These ratings are thus independent and mutually exclusive, and to the extent that they cover the range of potential severity, they are exhaustive. Assumption 3 is met as we consider that each individual participant was not reporting depressive symptoms during the prodromal period with any awareness as to their potential relation to those that would remain as residual symptoms, and vice versa. Thus, we can consider that the rater of the prodromal and residual symptoms was operating independently from his/her own influence during the other rating period. As such, the assumptions for Cohen's Kappa appear to be met in this study.

Hypothesis 2: Individuals will display similar durations of the prodromal and residual phases for a given episode.

To test this hypothesis, the correlation of the duration (in days) of the prodromal and residual periods for each episode of depression was computed as a Pearson Product Moment

Correlation (*r*). This correlation measures the extent to which one variable covaries with another, standardizing the variables when computing the covariance. The assumptions for such a correlation include: 1) interval or ratio scale data. The variables being correlated are the number of days spent in each period, which qualifies for interval level data. 2) Independent random sampling. This assumption is met in this study, as each pair of durations is presumably independent of the other pairs included in the analyses. Moreover, all pairs in the population should have an equal chance of being selected for the study, as the sample is large and representative of the young adult population. 3) There is a linear relationship between the variables. Assumption 4 addresses the normality of the distributions of both variables, and assumption 5 concerns the bivariate normality of the distribution of two variables together. Lastly, assumption 6 concerns the homoskedasticity (equal variances) of the variables. If certain assumptions for the Pearson Product Moment Correlation were not met (i.e., regarding the normality of the distributions), it's nonparametric alternative, the Spearman Rank correlation (ρ), would be conducted to assess the significance of the correlation of the ranks of the data. The significance of the correlation between the prodromal and residual period durations was evaluated to determine whether they are similar, as hypothesized, with $p < .05$ deemed significant.

Hypothesis 3: According to the rollback phenomenon, the sequence of prodromal symptom presentation will appear, in reverse, as the symptoms of depression remit.

To test this hypothesis, Spearman's rho (ρ) was computed on the order (ranks) of symptom onset and offset for a given episode. This can be thought of as the regular Pearson Product-Moment correlation coefficient (see above); that is, in terms of the proportion of variability accounted for, except that Spearman ρ is computed from ranks. As a nonparametric test, the primary assumption here is that the variables under consideration are measured on an ordinal (rank order) scale. Toward this end, symptoms of a given episode were ranked as to their

onset, with 1 being the first symptom present, and ties given to symptoms that began on the same day. Likewise, the order in which symptoms remitted was ranked, with 1 being the first symptom to remit, and ties given to symptoms that remitted on the same day. A negative correlation would be expected if the early symptoms were the last symptoms to remit. A value for ρ was calculated for each episode, with median and mean sample ρ's calculated from the ρ's from each individual episode. Values were interpreted loosely according to Landis and Koch (1977) as a measure of correlation, as no specific methods for interpreting Spearman's Rho correlations are available.

Hypothesis 4: Prodromal symptom profiles will be similar across successive prodromes of successive episodes.

To test this hypothesis for individuals experiencing more than one episode of depression during the course of the study, the prodromal symptom profiles for each pair of successive episodes of depression were compared using the same procedures to assess the similarity of prodromal and residual symptom profiles in hypothesis 1 (see above). Cohen's Kappa was calculated for successive episodes based on the presence or absence of the 29 SADS-C depression symptoms in each episode's prodromal phase. This yielded a measure of symptom agreement for each pair of successive prodromal phases. A mean sample κ was then calculated based on these κ's. The level of concordance of prodromal symptom profiles was considered according to the cutoffs proposed by Landis and Koch (1977).

Hypotheses 5-7: Specificity of the order of symptom onset and offset in hopelessness depressions.

To test these hypotheses that specific symptoms would be the first to appear and last to remit in hopelessness depressions, all depressions experienced during the course of the study were assessed according to the diagnostic criteria of hopelessness depression (HD) established by Alloy and colleagues (2006, appendix) for the CVD project. The symptoms present throughout

episodes of depression meeting these criteria for HD were subjected to survival analyses to determine whether a specific order of onset and offset of the symptoms occurred. Survival analyses (Elandt-Johnson & Johnson, 1980) of symptoms have been employed in previous studies of the order of symptom onset in seasonal affective disorder depressions (e.g., Young et al., 1991). In these studies, a survival analysis for each symptom provided an estimate of the symptom's probability density (risk of onset) for each week of an episode. These Kaplan-Meier probability estimates consist of the proportion of participants with the symptom beginning in each week. The probability density functions for each symptom can be graphed and compared, indicating which symptoms are more likely to appear before others. Moreover, the probability densities for the offset of a symptom could likewise be ascertained to identify the relative order in which symptoms remit. Survival analysis is appropriate for the current study, as it accounts for: 1) data which consist of time to an event (symptom onset or offset); 2) data which are censored by the fact that the event did not occur for all participants during the period of observation; and 3) data which are censored by the fact that the period of observation varied across participants.

For the purposes of the current study, the probability densities for the onset and offset of the 29 SADS-C symptoms were ascertained for 3-day periods beginning with the appearance of the first (prodromal) symptom and ending with the offset of the last symptom to remit. Three-day periods were utilized as preliminary observation of the data indicated that often times, several symptoms appeared in the same week. Breaking the time period down to a shorter interval increased the ability to accurately identify a pattern of symptom onset, if symptoms appear in the same week, and could address situations in which the depression progresses rapidly, with new symptoms appearing shortly after one another. For prodromal symptoms, the onset of the first symptom served as time 0 for each individual, and the onset of subsequent symptoms was coded in subsequent 3-day intervals. Probability density graphs represent the likelihood of a given symptom appearing during a particular 3-day period. In these graphs, time 0 represents the first

prodromal symptom to appear and symptoms with probability density graphs that are initially high and rapidly declining over time represent symptoms that are most likely to appear early in the prodrome.

For the remission of symptoms, the date of offset of the last symptom to remit served as time 0 for each individual, and the offset of preceding symptoms was coded in preceding 3-day intervals corresponding to the number of days the symptom remitted before the last symptom. Such a reverse-coding procedure was used to standardize the endpoint of the remission period across participants, to address the possibility that periods of residual symptoms can vary across individuals. Otherwise, coding the first symptom to remit as time 0 and subsequently coding remitting symptoms could generate misleading probability density curves, as different individuals could have the same sequence of symptom offset, but if one happens more rapidly than the other, the probability density graphs for the symptoms would not be representative of this. As the hypotheses being tested are especially interested in the later symptoms to remit, standardizing the endpoint as the last symptom to remit strengthens the survival analyses' ability to identify the sequence of symptom offset closer to the end of the depression. Additionally, such a procedure generates probability density graphs that can be more easily compared with the graphs for symptom onset, increasing the ability to address the hypotheses in question. In these graphs, the time is the difference between the last symptom to remit and when the symptom in question remitted. Thus, time 0 indicates the time that the last symptom remitted; later times actually represent more time between symptom remission and the end of the remission phase- these symptoms are remitting earlier. Accordingly, as with symptom onset graphs, graphs with initially high and rapidly declining probability density functions represent symptoms that are most likely to remit at the end of the remission phase (there is less time between the symptom remission and the end of the remission phase).

Statistical tests of the differences between probability density graphs were not conducted because there did not appear to be a clear method of doing so. Thus, the survival analyses employed to test these hypotheses were descriptive rather than inferential statistics. Other survival techniques (e.g. Cox regression) make assumptions that are not applicable to the data involved in the current study, as the curves in question did not represent different participant groups, but different symptoms within the same participants. Indeed, previous studies of the pattern of depressive symptom onset (Young et al., 1991) did not statistically test for differences in rates for the same reasons.

Alternative tests of these hypotheses concerning hopelessness depression symptoms were conducted by grouping participants according to their cognitive risk status (HR vs. LR). The rationale for these tests is that the participants demonstrating a negative cognitive style (HR participants) would be more likely to develop hopelessness, and the other symptoms of hopelessness depression, than LR participants, as they employ negative cognitive styles when inferring the causes and implications of negative life events (e.g., Abramson et al., 1989). Survival analyses following the same procedure outlined above were conducted on each of the 29 SADS-C symptoms for both the HR and LR groups, and statistical tests of interactions between group and symptoms were conducted, to test for differences in survival rates for symptoms between the HR and LR groups. As with the probability density graphs, these survival curves represent the difference in time between the first symptom to appear and the emergence of the symptom in question, and the difference in time between the last symptom to remit and the remission of the symptom in question. Accordingly, time 0 represents the earliest symptom to appear in survival curves of symptom onset, and time 0 represents the last symptom to remit in survival curves of symptom remission.

Hypotheses 8-9: Specificity of the order of symptom onset and offset in endogenous depressions.

A procedure analogous to that employed to test hypotheses 5-7 concerning hopelessness depression was employed to test hypotheses 8-9 concerning endogenous depression. All depressions experienced throughout the study were assessed to determine if they met RDC criteria for endogenous depression, based on SADS-C assessment. These SADS-C symptoms include: loss of interest or pleasure, depressed mood, feelings of guilt, middle insomnia, early awakening, psychomotor retardation or agitation, poor appetite, weight loss and suicidal ideation. These are the symptoms that are hypothesized to appear earliest and remit latest in episodes that meet criteria for endogenous depression in this study. The symptoms present throughout episodes of depression meeting criteria for endogenous depression were subjected to survival analyses, according to the same procedure outlined above, to determine whether a specific order of onset and offset of the symptoms appeared.

Hypotheses 10-11: Differences in the pattern of symptom onset and offset between individuals at high and low levels of sociotropy.

To test this hypothesis, individuals were grouped as follows: High Sociotropy (HS; the upper 33% of scorers on the SAS Sociotropy scale) and Low Sociotropy (LS; the lowest 33% of scorers on the SAS Sociotropy scale). The upper and lower 33% groups were selected because they represent the extreme levels of sociotropy in the sample, and should therefore demonstrate the most powerful effects of sociotropy on symptom expression. Following the grouping of participants, survival analyses following the same procedure for testing hypotheses 5-9 above were conducted, comparing survival rates between the HS and LS groups to determine if differences in prodromal and residual symptom patterns emerged. It was hypothesized that the symptoms assessed in the SADS-C and empirically associated with sociotropy in past studies (self blame, psychomotor agitation, crying more, worrying/brooding and decreased self-esteem)

would be the earliest to appear and latest to remit among HS participants as compared to LS participants.

Hypotheses 12-13: Differences in the pattern of symptom onset and offset between individuals at high and low levels of autonomy.

To test this hypothesis, individuals were grouped as follows: High Autonomy (HA; the upper 33% of scorers on the SAS Autonomy scale) and Low Autonomy (LA; the lowest 33% of scorers on the SAS Autonomy scale). Procedures for testing the pattern of symptom onset and offset between these groups was analogous to those employed to test hypotheses 10-11 above, utilizing survival analyses to test for differences in survival rates of symptom onset and offset between the HA and LA groups. It was hypothesized that the symptoms assessed on the SADS-C and empirically associated with autonomy in past studies (decreased interest or pleasure, suicidal ideation, hopelessness and irritability) would be the earliest to appear and latest to remit among HA participants as compared to LA participants.

CHAPTER 3
RESULTS

In this study a total of 331 episodes of depression were analyzed. The final sample included 160 participants from the Temple-Wisconsin Cognitive Vulnerability to Depression (CVD) Project that experienced at least one depressive episode during the 2.5-year prospective study period. This consisted of 96 cognitive high-risk and 64 cognitive low-risk participants; 96 were from the University of Wisconsin and 64 were from Temple University. The mean age at study entry was 18.69 years (s.d. 1.44 years). The sample was 71.8% female and 87.5% Caucasian. The mean SAS sociotropy score was 77.9 (33^{rd} percentile= 68.0, 67^{th} percentile= 89.0). The mean SAS autonomy score was 96.53 (33^{rd} percentile= 91.96, 67^{th} percentile= 100.15). Table 1 provides the demographic characteristics of this sample.

Across the 331 episodes analyzed in this study, the mean number of prodromal symptoms experienced was 3.73 (median= 3.0) and 27 episodes did not exhibit a prodromal phase. The mean number of residual symptoms was 3.82 (median= 3.0) and 25 episodes did not exhibit a residual phase. 16 episodes demonstrated only an acute phase- no prodromal or residual symptoms. This implies that a large majority of the episodes in this sample consisted of a prodromal, acute and residual phase. There were 45 episodes in which there was only 1 prodromal symptom and 32 episodes with only 1 residual symptom; there were 21 episodes with 1 prodromal and residual symptom. This is important insofar as the presence of only 1 prodromal or residual symptom could lead to perfect concordance in the analyses of symptom concordance conducted for hypothesis 1. However, given the large number of episodes analyzed and the relatively small number of episodes with only 1 prodromal or residual symptom, it is unclear whether this is meaningful to the analyses.

Table 1.
Demographic Characteristics of the Sample

	High Risk	Low Risk
	Temple Site	
Sample Size	37	27
Age	18.59 (1.52)	19.37 (2.23)
Ethnicity	78.4% Caucasian	70.3% Caucasian
Gender	64.9% Female	77.8% Female
	Wisconsin Site	
Sample Size	59	37
Age	18.44 (.50)	18.68 (1.55)
Ethnicity	98.3% Caucasian	91.9% Caucasian
Gender	72.4% Female	75.6% Female

Note. Standard deviations in parentheses.

Preliminary Analyses:

To support the existence and relevance of the prodromal phase of a depressive episode, the number of SADS-C symptoms present immediately before and leading into the acute phase of a depressive episode was compared to the number of SADS-C symptoms present for similar periods of time for non-depressed CVD participants. Toward that end, 60 participants from the final sample were matched with participants from the CVD Project who did not experience an episode of depression, on the basis of age, gender, ethnicity and cognitive risk status. Congruent with the hypothesis, depressed participants had a significantly greater number of symptoms

during this prodromal period than non-depressed, matched participants (3.73 vs. 1.50 symptoms; $t(212)= -6.203$, $p < .001$). Further, χ^2 analyses were conducted on the presence of each of the SADS-C symptoms during this period between participants who developed a depressive episode and those who did not. Nine symptoms were found to be significantly more likely to be present among the depressed participants than the non-depressed participants. These were: depressed mood ($\chi^2(1) = 23.821$, $p< .001$), decreased interest in or pleasure from activities ($\chi^2(1) = 11.006$, $p< .001$), self blame ($\chi^2(1) = 4.693$, $p< .025$), decreased concentration ($\chi^2(1) = 6.755$, $p< .008$), hopelessness ($\chi^2(1) = 51.011$, $p< .001$), worrying/brooding ($\chi^2(1) = 8.702$, $p< .003$), decreased self-esteem ($\chi^2(1) = 31.126$, $p< .001$), irritability ($\chi^2(1) = 9.062$, $p< .002$) and increased dependency ($\chi^2(1) = 5.894$, $p< .013$).

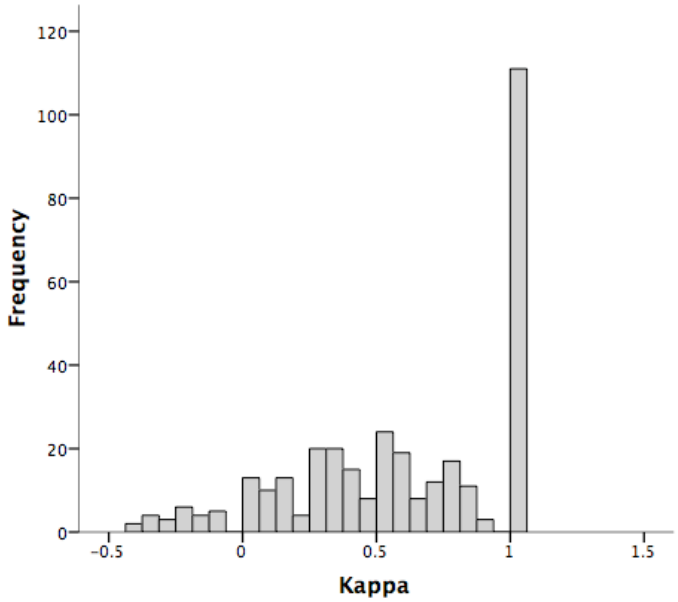
Hypothesis 1:

Cronbach's κ was calculated as a measure of concordance of prodromal and residual symptoms for each episode of depression. Figure 2 displays the distribution of κ's observed. Since the distribution is not a normal one, and is influenced by a number of 1.0 scores, the median is presented as a more robust measure of the central tendency of the data than the mean. Across all episodes, the median $\kappa= .605$ (mean= 0.585, mode= 1.0).

Hypothesis 2:

The correlation between the durations of prodromal and residual phases was conducted for each episode in the sample. The mean duration of the prodromal phase was 44.75 days (s.d. = 39.73 days) and of the residual phase was 36.39 days (s.d = 27.05 days). The correlation was calculated as $r(329)= .385$. However, exploration of the data revealed that the assumptions for the significance test for the Pearson Product Moment correlation were not all met. Specifically, there were numerous outliers among both the prodromal and residual duration variables and their distributions were found to be non-normal (Shapiro-Wilk test of departure from normality yielded

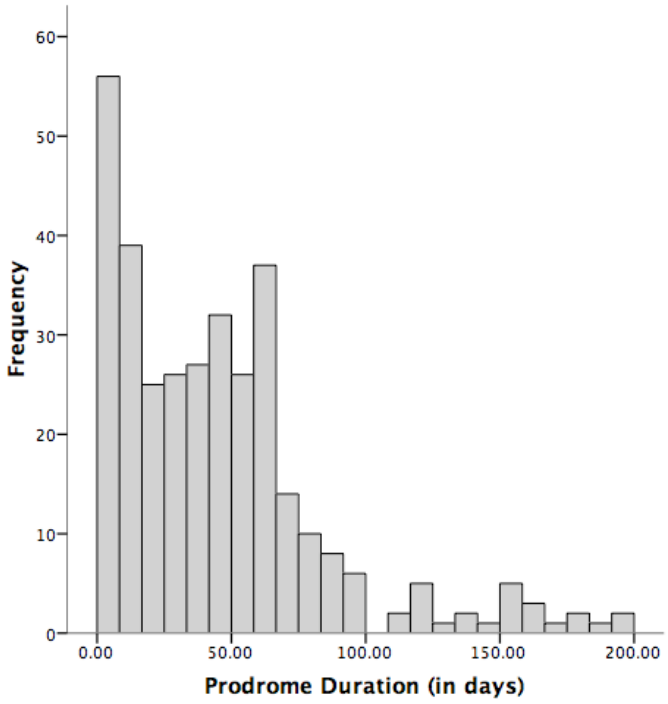
Figure 2. Distribution of Kappas for the Concordance of Prodromal and Residual Symptomatology.

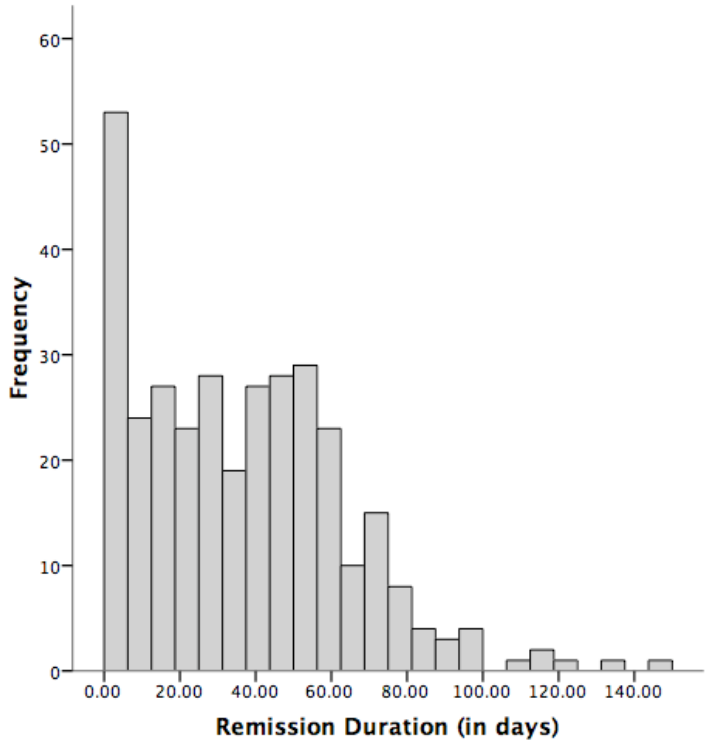


$p < .001$ for both variables). Figure 3 displays a graphical representation of the distribution and outliers. Given that the normality assumption of the distribution of these variables was not met and the presence of numerous outliers, the nonparametric alternative, the Spearman rank correlation (ρ), was computed to assess the significance of the correlation of the ranks of the data. The correlation was found to be moderate and significant, with $\rho(329) = .486$, $p < .001$.

For episodes that had both a prodromal and residual phase (no "0" values), the results were very similar. The mean duration of the prodromal phase was 48.99 days (s.d. = 38.71 days) and of the residual phase was 39.55 days (s.d = 25.62 days). The correlation was calculated as $r(295) = .358$. Here too, the assumptions for the significance test for the Pearson Product Moment correlation were not all met. There were numerous outliers among both the prodromal and residual duration variables and the distributions of both variables were found to be non-normal

Figure 3. Distribution of the Prodromal and Remission Phase Durations (in Days).





(Shapiro-Wilk test of departure from normality yielded $p < .001$ for both variables). The Spearman rank correlation (ρ) was computed to assess the significance of the correlation of the ranks of the data. The correlation was found to be moderate and significant, with $\rho(295) = .431$, $p < .001$.

Hypothesis 3:

Spearman's rho was calculated for each episode of depression to determine the correlation of the order of symptom onset and remission. The distribution of these correlation coefficients was not normally distributed, with a substantial number of -1.0 correlations. See Figure 4 for a display of the distribution of Spearman's rho (ρ) scores. As such, the median is presented as a more robust measure of the central tendency of these data, as opposed to the mean. The median correlation of the order of symptom onset and remission was $\rho = -0.642$ (mean= -0.564, mode= -1.0).

Hypothesis 4:

Eighty-one participants experienced more than 1 episode of depression during the prospective assessment period of the CVD Project, yielding a total of 252 episodes of depression. Of these participants, 56 were from the University of Wisconsin site and 26 were from Temple University. Fifty-seven of the 81 (70.0%) were classified as cognitive HR participants.

Cohen's Kappa (κ) was calculated as a measure of the concordance of prodromal symptom profiles for each pair of successive episodes of depression for each participant. Kappas for each pair of successive episodes were then averaged for each participant. Participant mean kappas ranged from -.258 to 1.0. Figure 5 provides a display of the distribution of these participant mean κ scores. Across participants, the mean value for the concordance of prodromal symptom profiles across successive episodes of depression was $\kappa = .40$ (median= .338, mode= 1).

Figure 4. Distribution of Spearman's Rho Correlations for the Order of Symptom Onset and Offset.

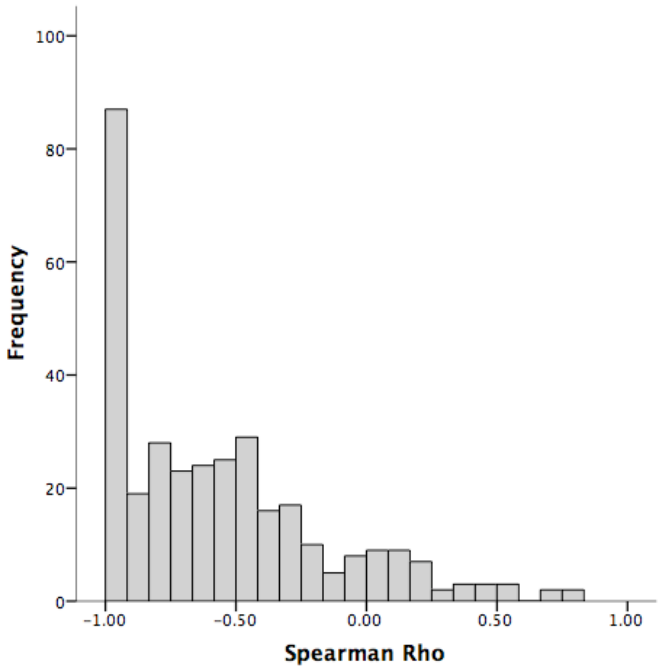
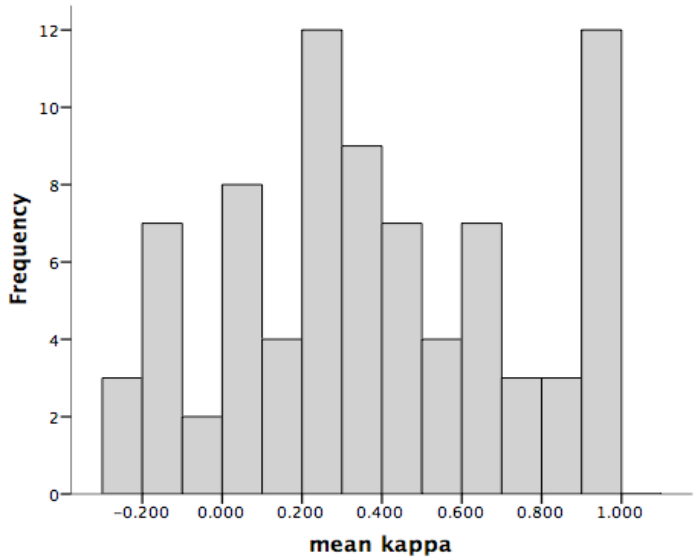


Figure 5. Distribution of Participant Mean Kappas for Symptom Agreement Across Prodromes.



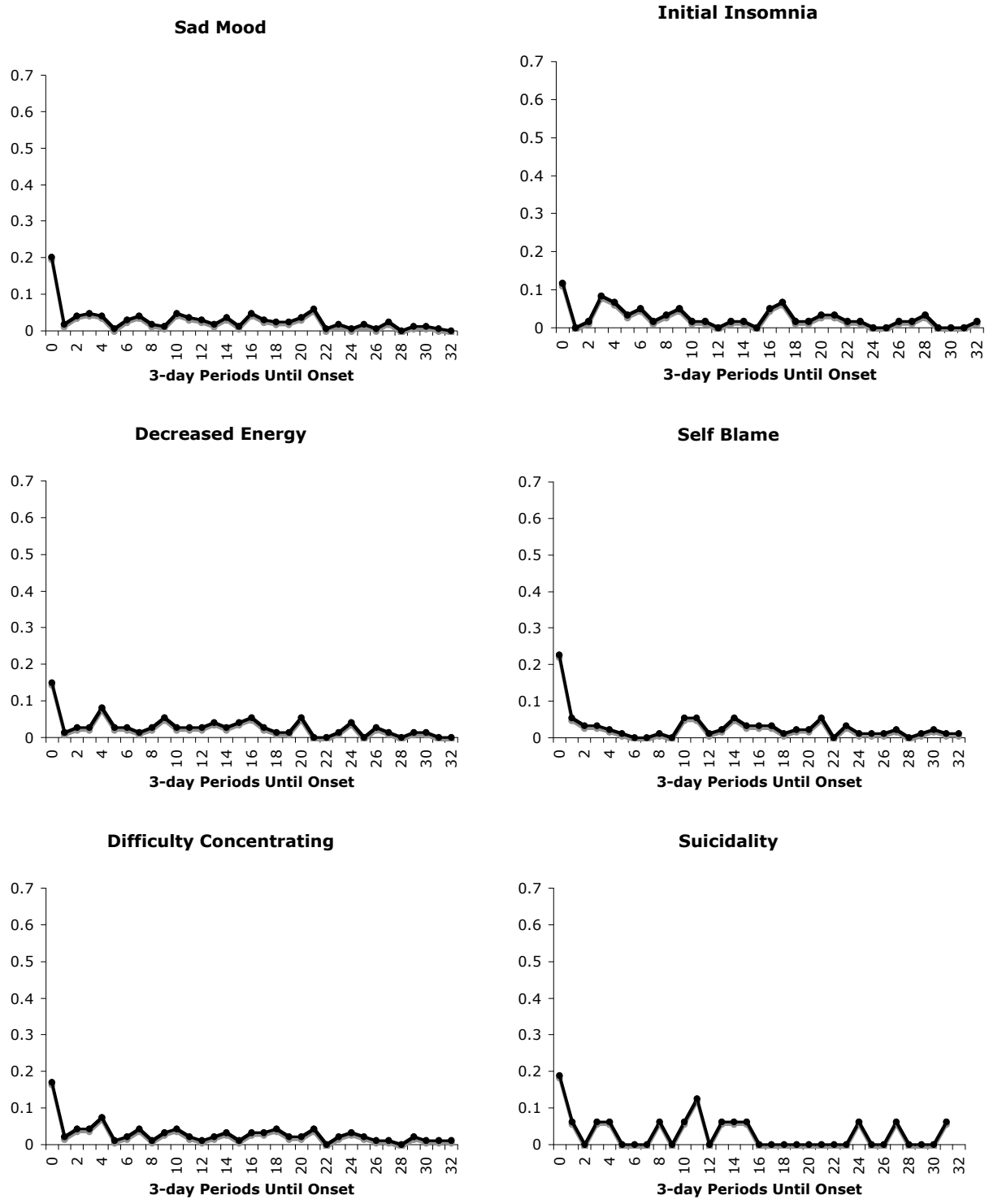
Hypotheses 5-7:

There were 169 episodes of depression that met criteria for hopelessness depression. These episodes were subjected to survival analyses for each symptom experienced during the prodromal, acute or remission phase. Survival analyses of each symptom yielded probability densities (risk of onset) for each 3-day period from the onset of the prodromal period, which were then graphed to display the likelihood of the symptom occurring over time. Figure 6 presents the probability density functions for the onset of each symptom experienced in a hopelessness depression. Visual inspection of the graphs indicates that the functions were of two characteristic shapes. The symptom of hopelessness appeared to have the most drastically declining probability density function of all the symptoms assessed. Sad mood, self blame, brooding/worry, decreased self-esteem, dependency and decreased appetite had initially high and generally declining probability densities as well. Linear and relatively constant probability density rates were observed for the other symptoms.

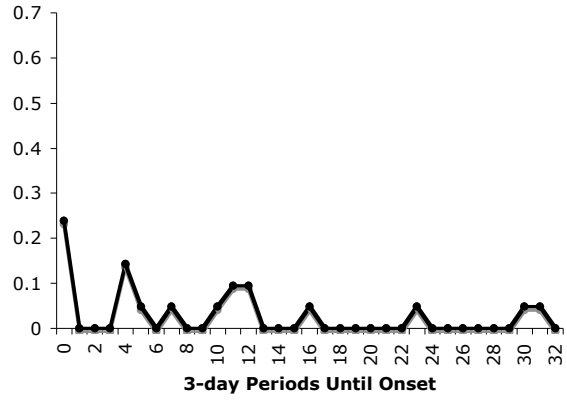
Survival analyses for each symptom experienced during a hopelessness depression also yielded probability densities for each 3-day period from the symptom offset to the end of remission, which were graphed and analyzed. Figure 7 presents the probability density functions for the offset of each symptom. Visual inspection of the graphs indicates that the symptoms of hopelessness and decreased self-esteem appeared to have the most drastically declining probability density functions of all the symptoms assessed. The functions for sad mood, self blame, brooding/worry, dependency and increased appetite had initially high and generally declining probability

Figure 6. Probability Density Functions for Symptom Onset in Hopelessness Depressions.

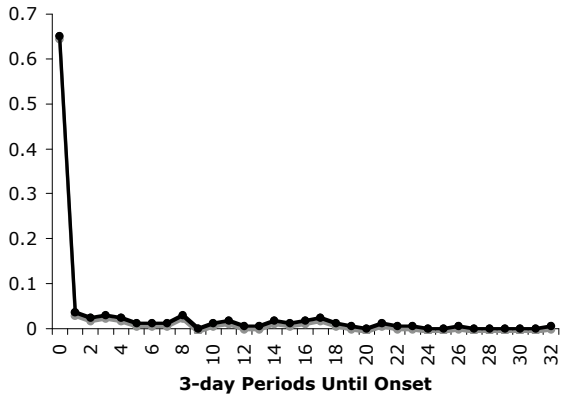
Hopelessness Depression Symptoms:



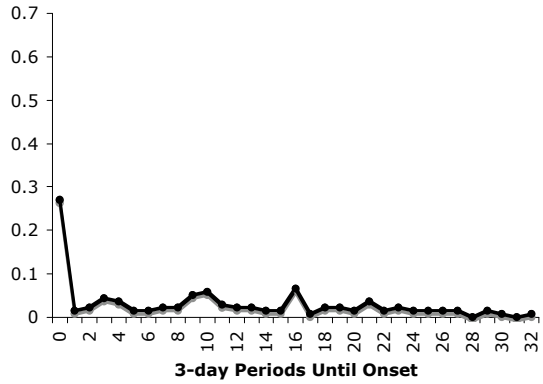
Psychomotor Retardation



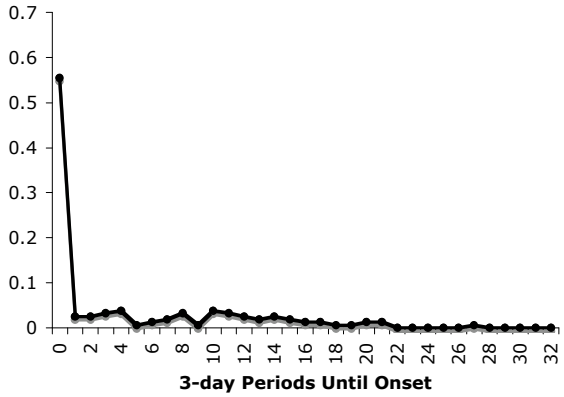
Hopelessness



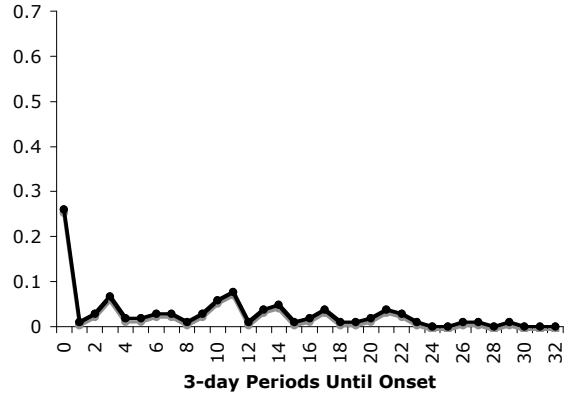
Broodying / Worry



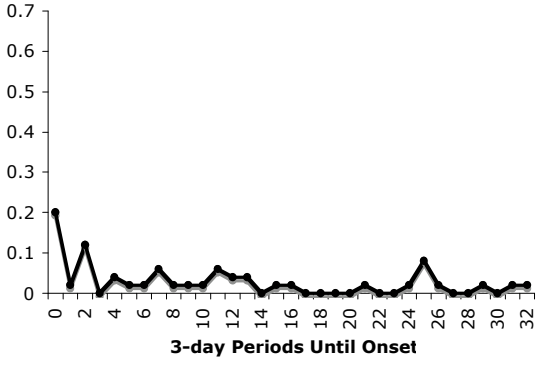
Decreased Self-Esteem



Dependency



Decreased Initiation of Voluntary Responses



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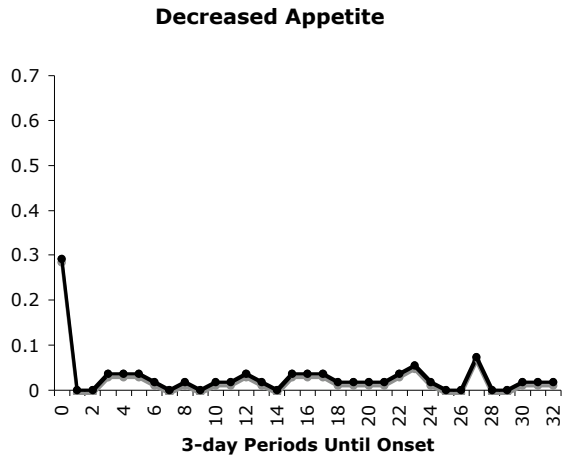
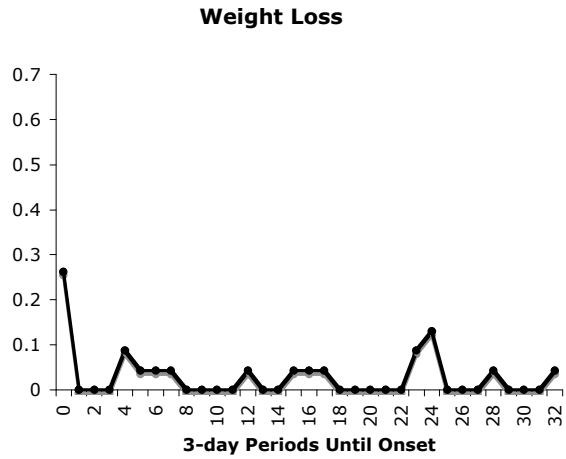
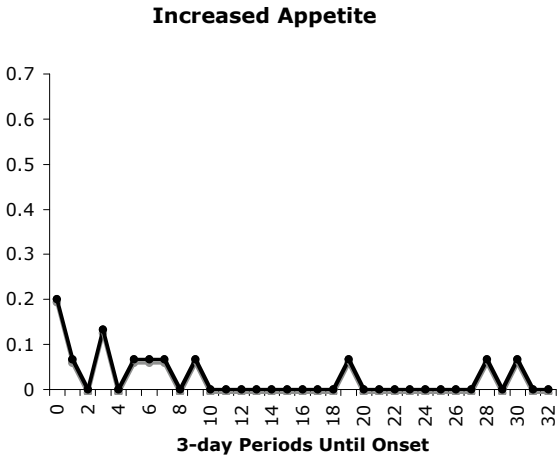
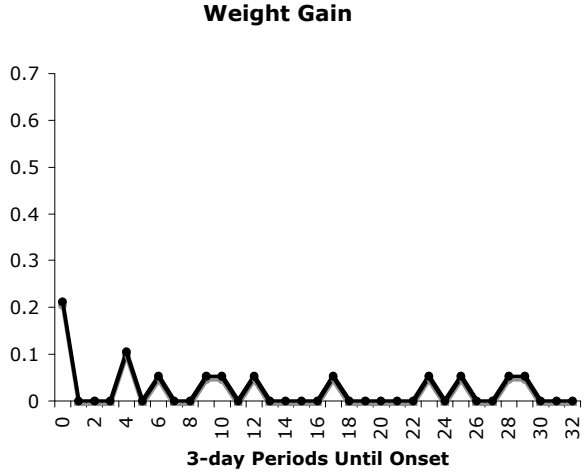
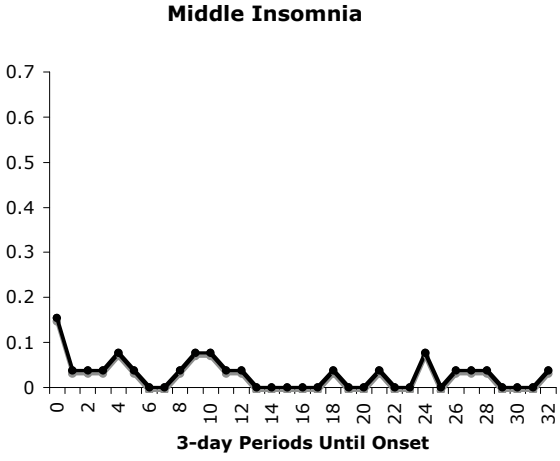
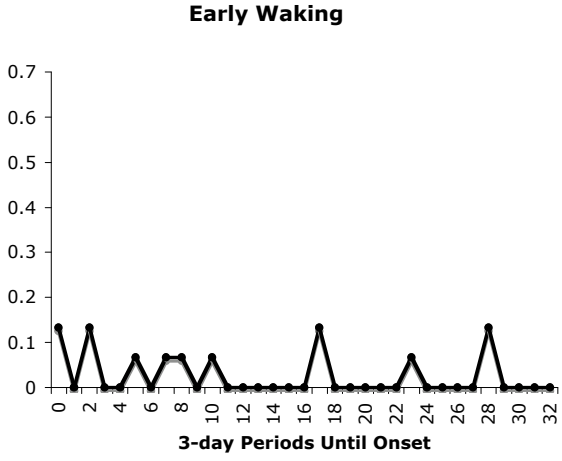




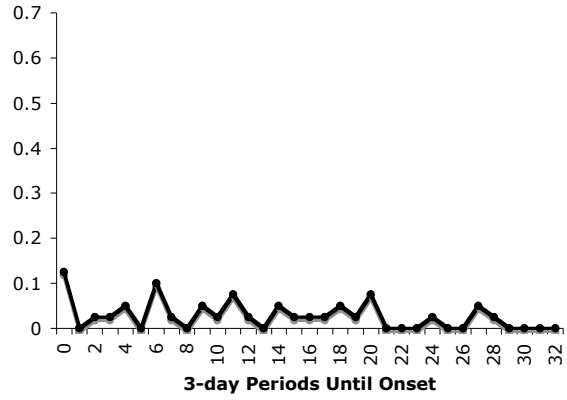




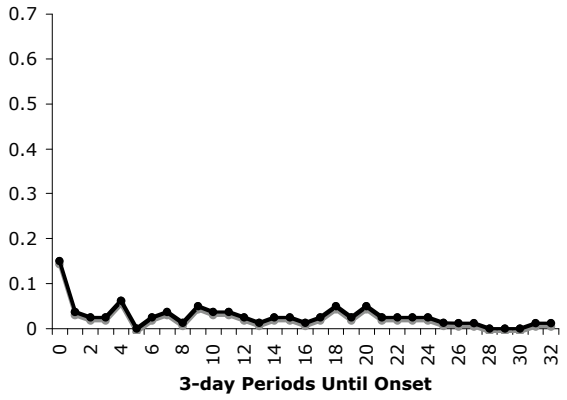




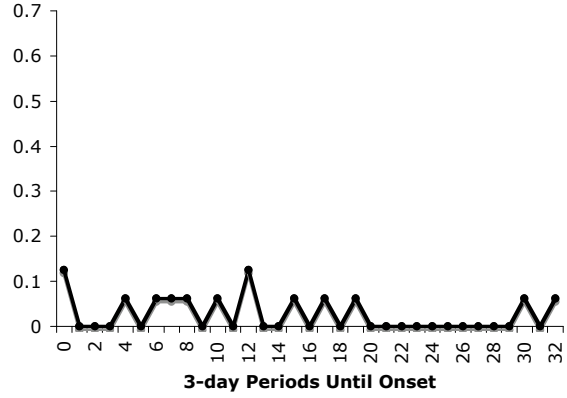
Hypersomnia



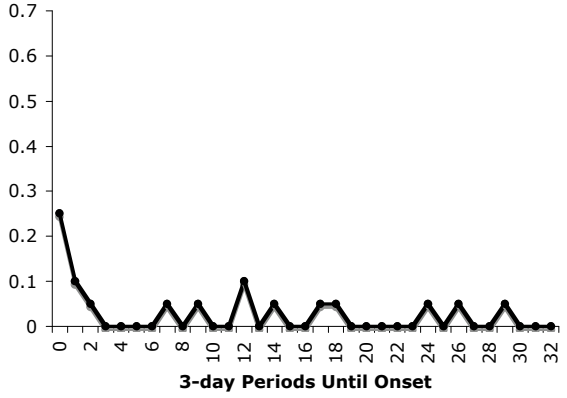
Decreased Interest or Pleasure



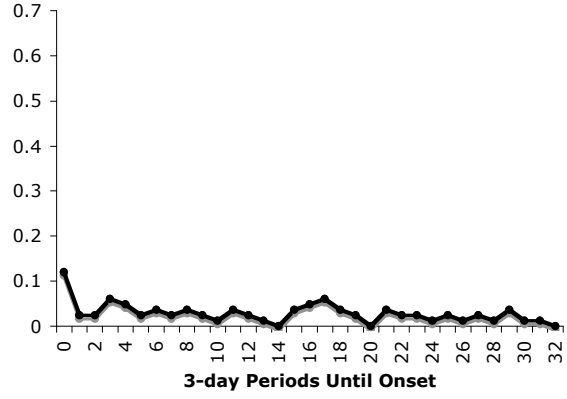
Psychomotor Agitation



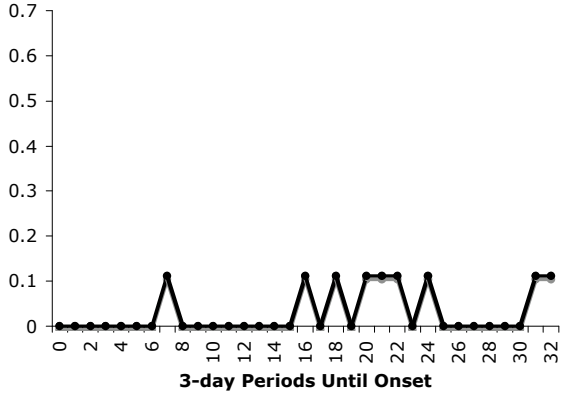
Indecision



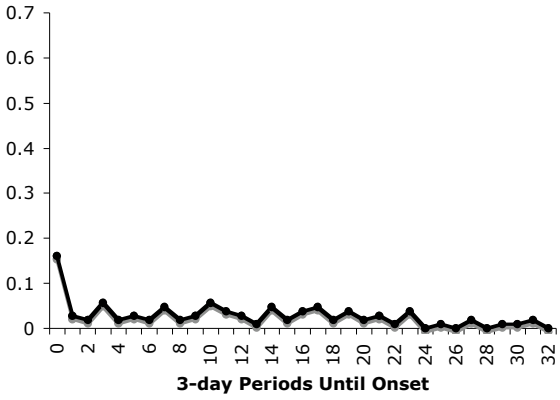
Crying



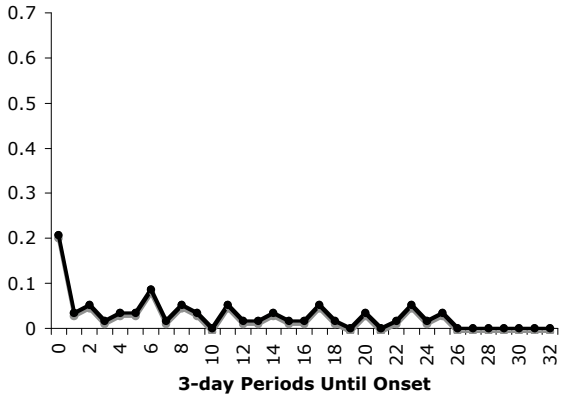
Inability to Cry



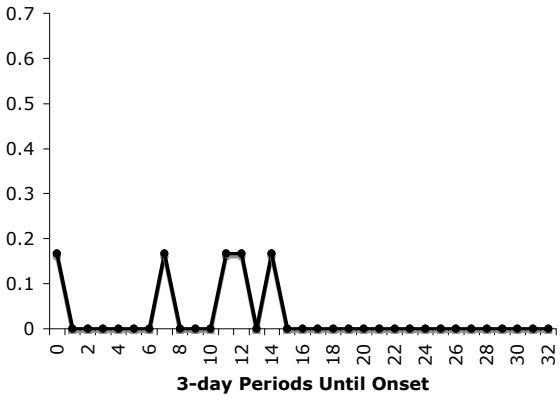
Irritability



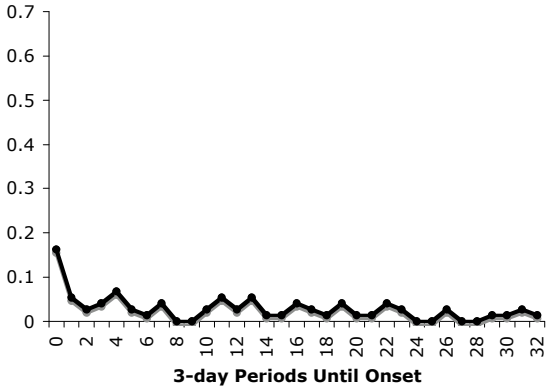
Self Pity



Somatic Complaints



Decreased Effectiveness



Helplessness

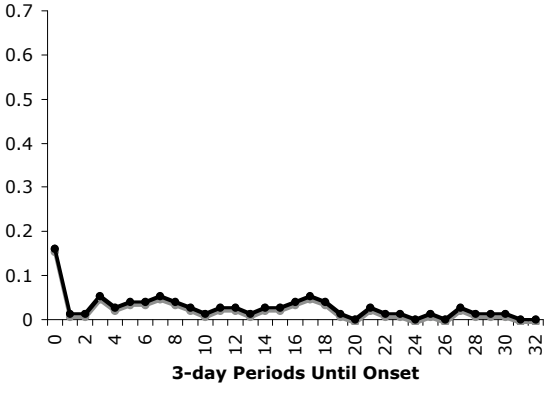
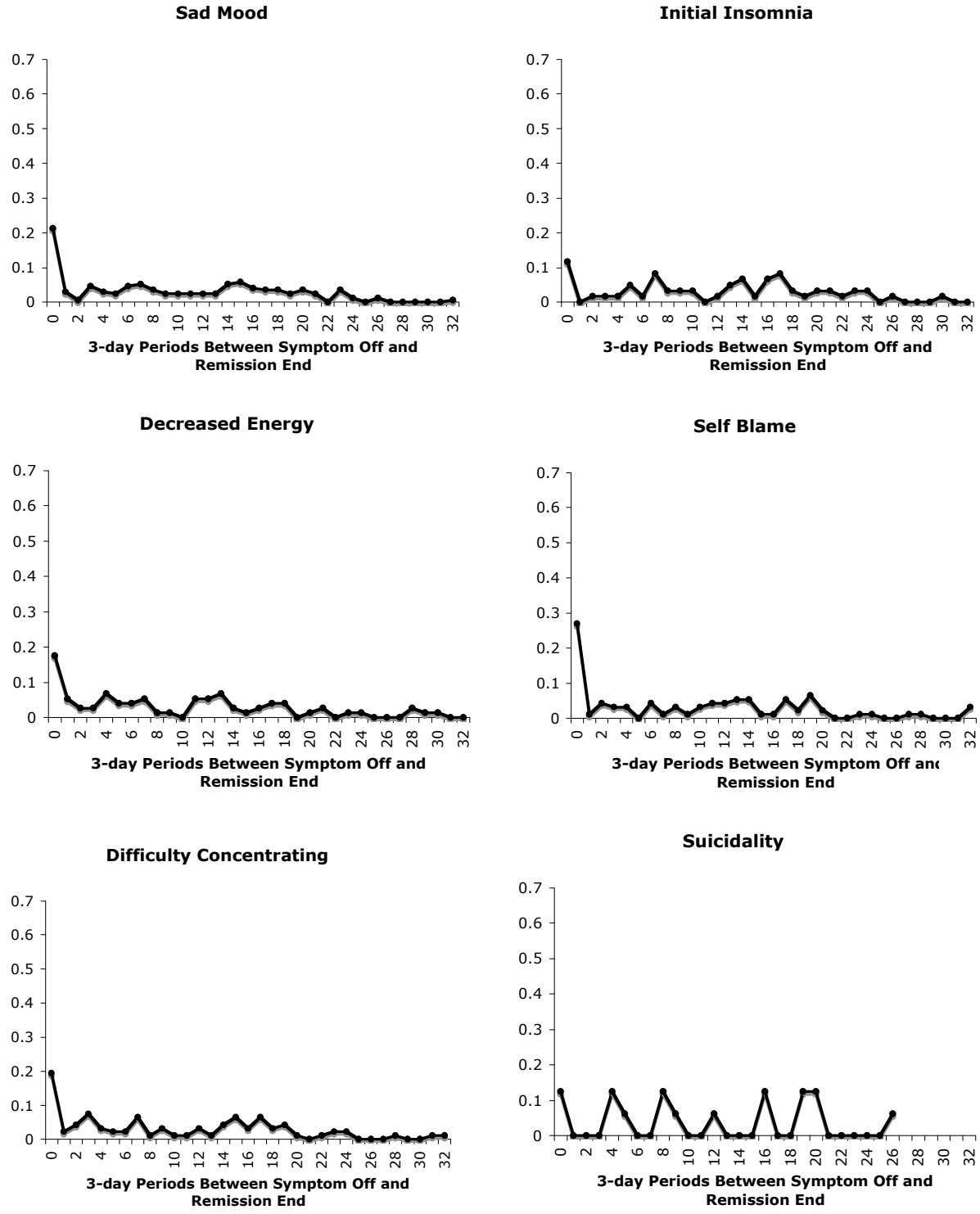
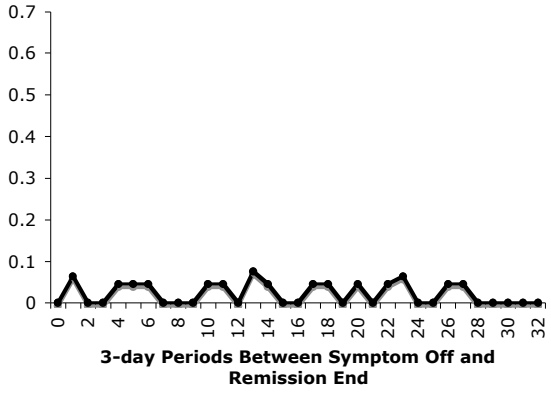


Figure 7. Probability Density Functions for Symptom Remission in Hopelessness Depressions.

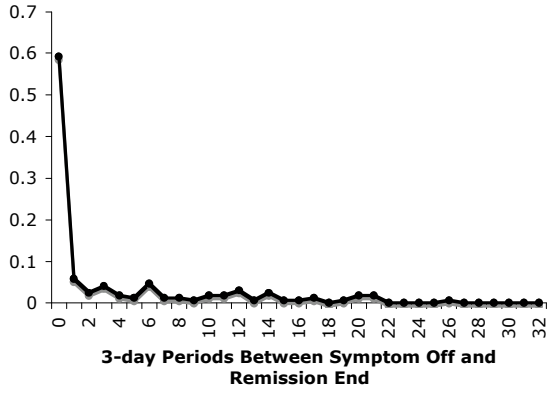
Hopelessness Depression Symptoms:



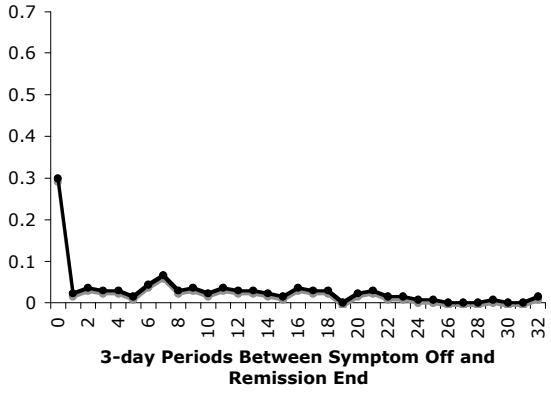
Psychomotor Retardation



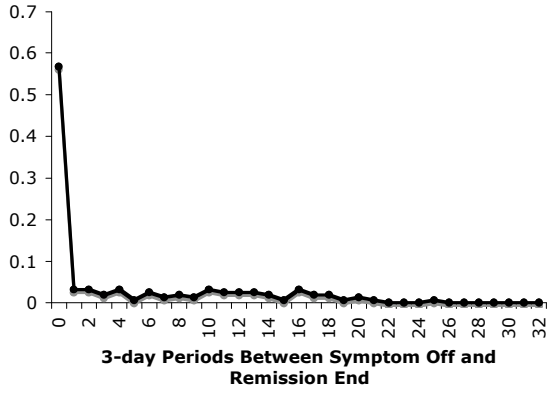
Hopelessness



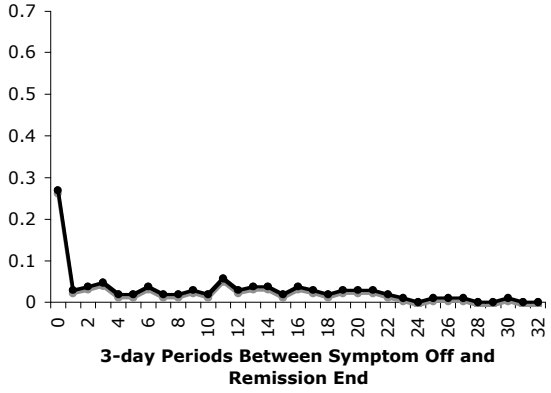
Brooding / Worry



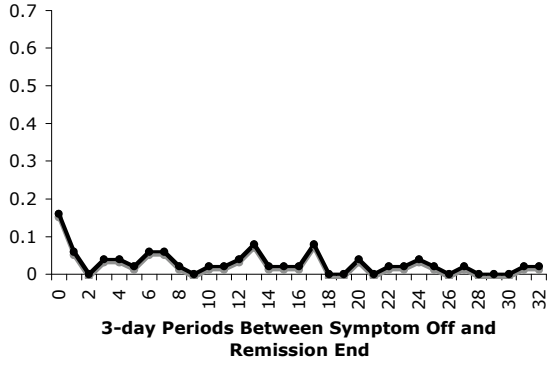
Decreased Self-Esteem



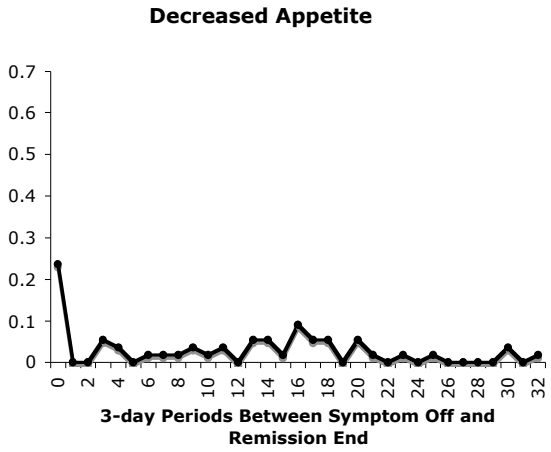
Dependency

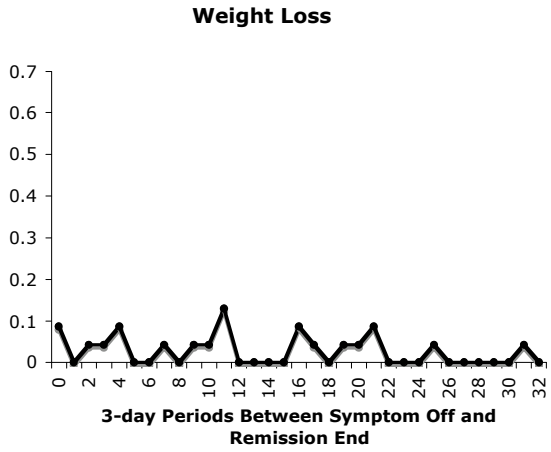


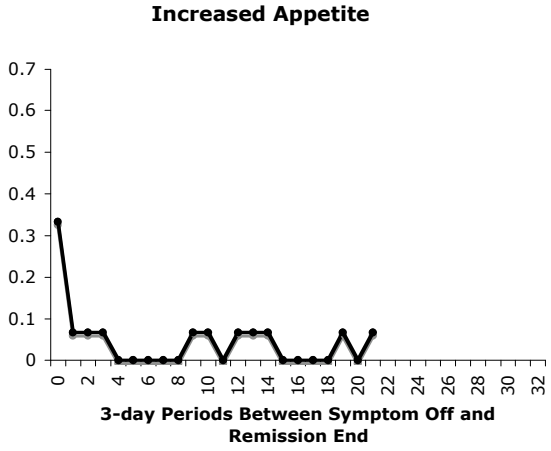
Decreased Initiation of Voluntary Responses

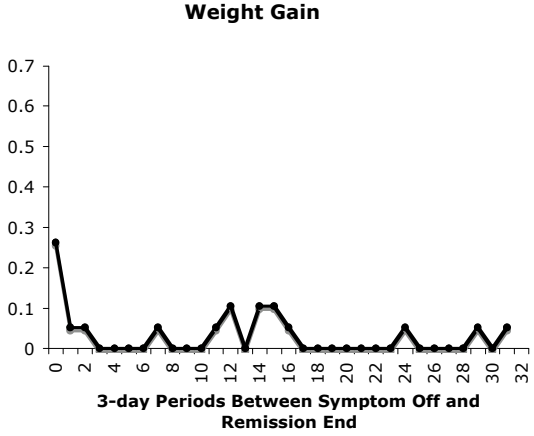


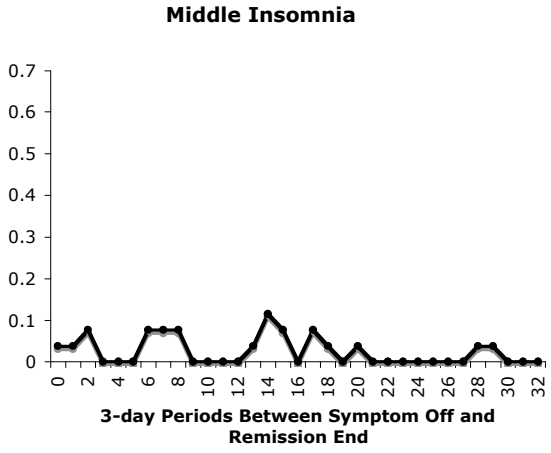
Other Symptoms:

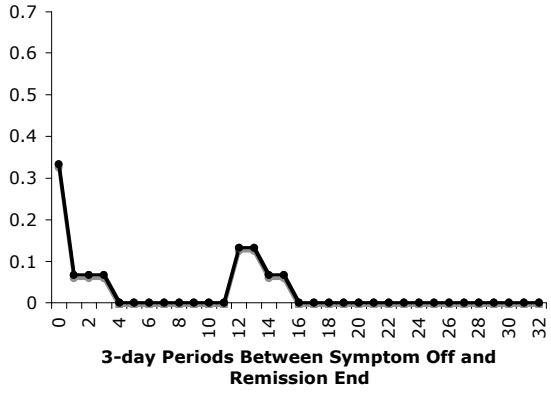




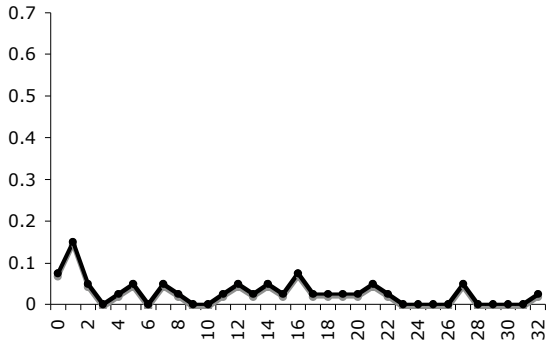




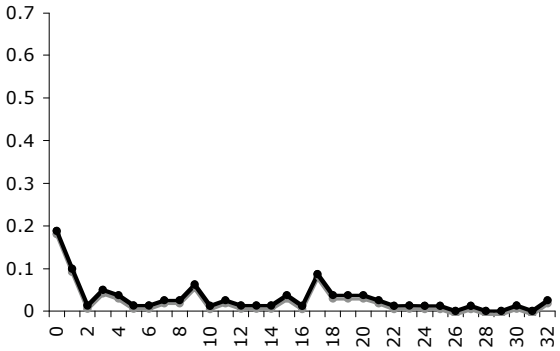




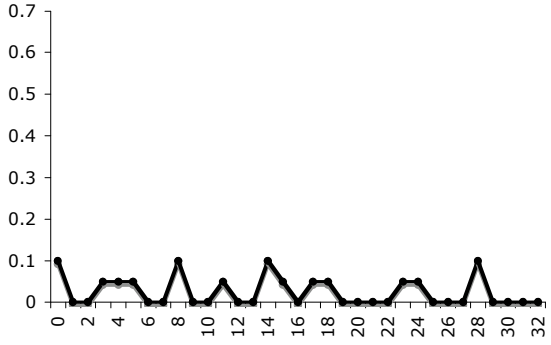
Hypersomnia



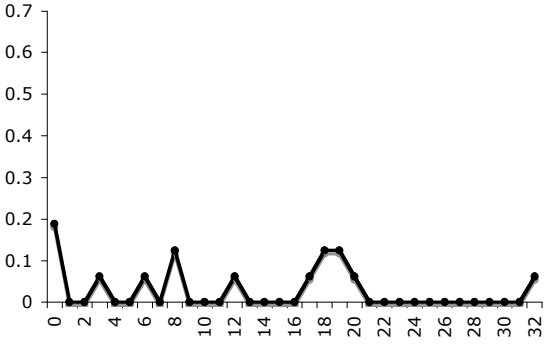
Decreased Interest or Pleasure



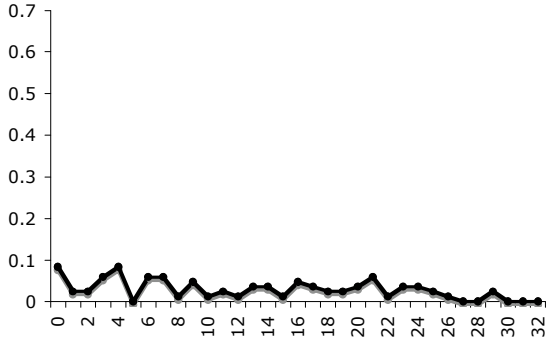
Indecision



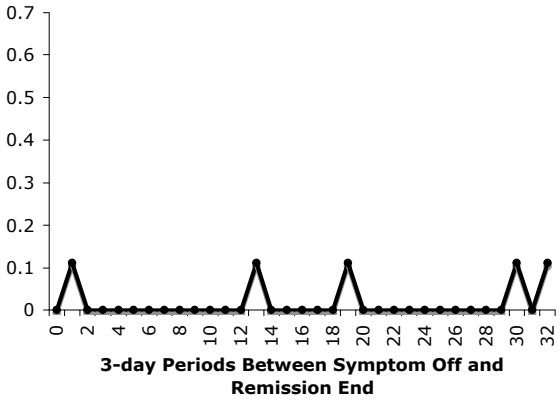
Psychomotor Agitation



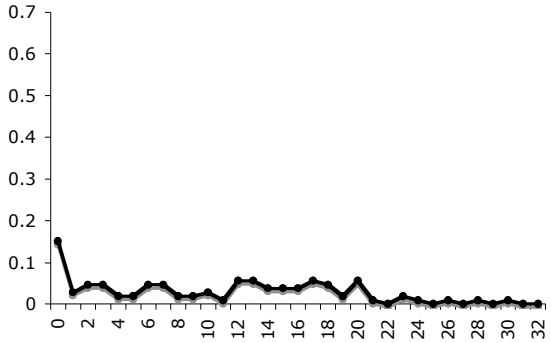
Crying



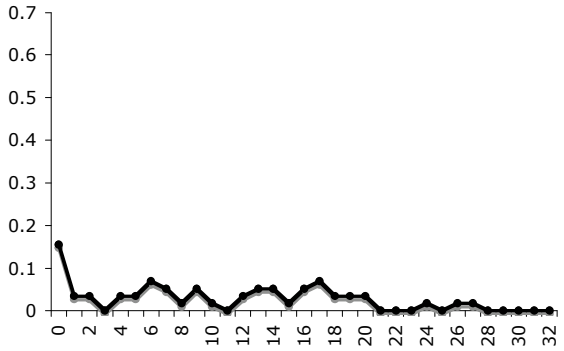
Inability to Cry



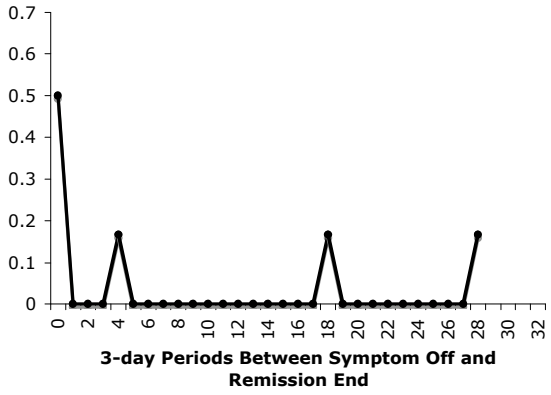
Irritability



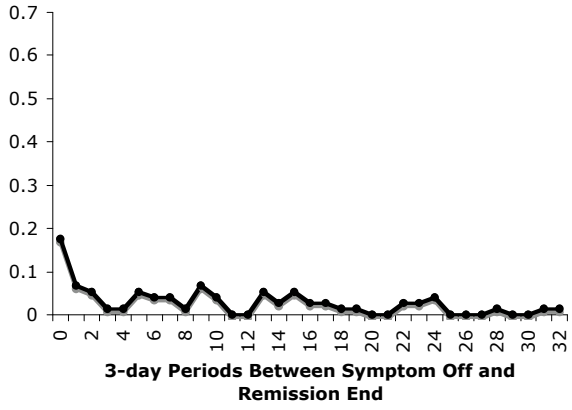
Self-Pity



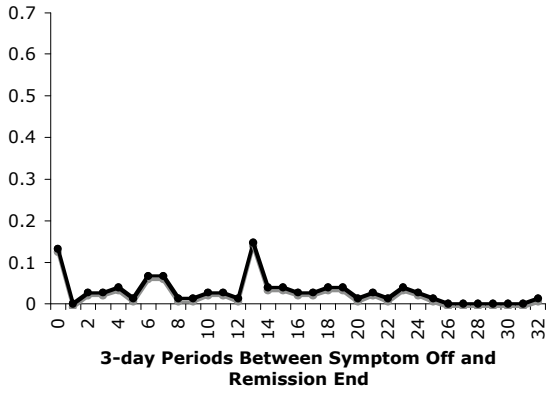
Somatic Complaints



Decreased Effectiveness



Helplessness

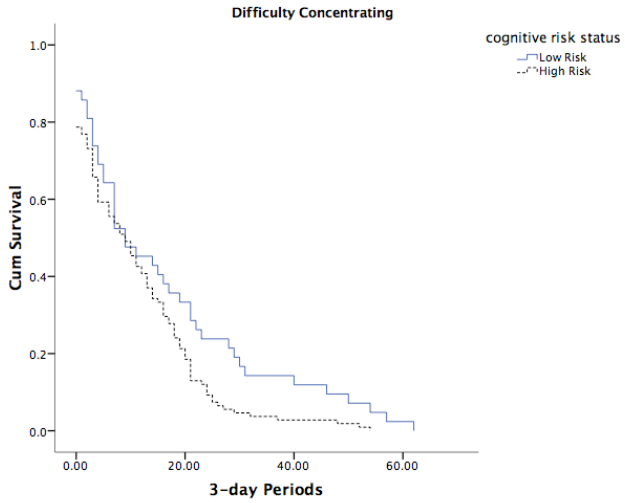


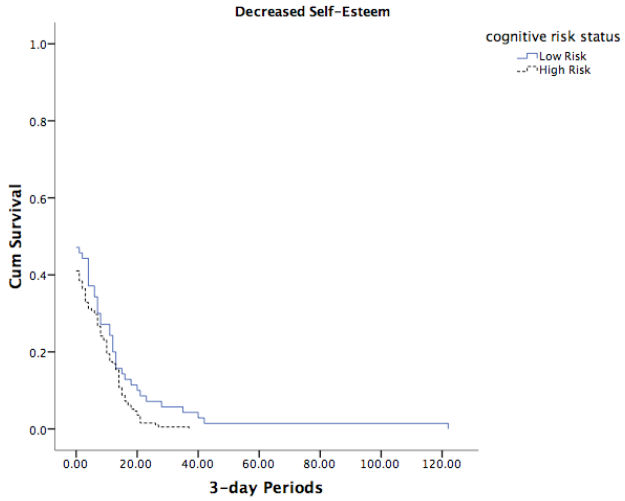
densities as well. The other symptoms had generally linear and relatively constant probability density graphs.

Survival analyses were conducted on each symptom's time to onset (in 3-day intervals) and survival curves compared across cognitive high- and low-risk groups. Log-rank analyses suggested significantly different survival curves for the onset of concentration difficulties ($\chi^2(1) = 4.894$, $p < .027$), decreased self-esteem ($\chi^2(1) = 3.884$, $p < .049$) and dependency ($\chi^2(1) = 10.865$, $p < .001$). Figure 8 displays the survival curves for both groups on each of these symptoms. These survival curves indicate that the onset of each of these symptoms was sooner for HR than LR participants. No other symptoms were found to have statistically different survival curves for symptom onset in hopelessness depressions.

Survival analyses were conducted on each symptom's time between offset and end of the remission phase (in 3-day periods) and survival curves compared across cognitive high- and low-risk groups. Log-rank analyses suggested significantly different survival curves for the offset of initial insomnia ($\chi^2(1) = 4.452$, $p = .035$), decreased energy ($\chi^2(1) = 3.751$, $p = .05$), suicidal ideation ($\chi^2(1) = 4.788$, $p = .029$) and decreased initiation of voluntary responses ($\chi^2(1) = 4.519$, $p = .034$). Figure 9 displays the survival curves for both groups on each of these symptoms. As demonstrated in each of these survival curves, the time between symptom remission and the end of the remission phase is shorter (indicating that the symptom remits closer to the end of the remission phase) for HR than LR participants. No other symptoms were found to have statistically different survival curves for the time between symptom offset and the end of the remission phase.

Figure 8. Survival Curves for Time to Symptom Onset in HR and LR Participants.





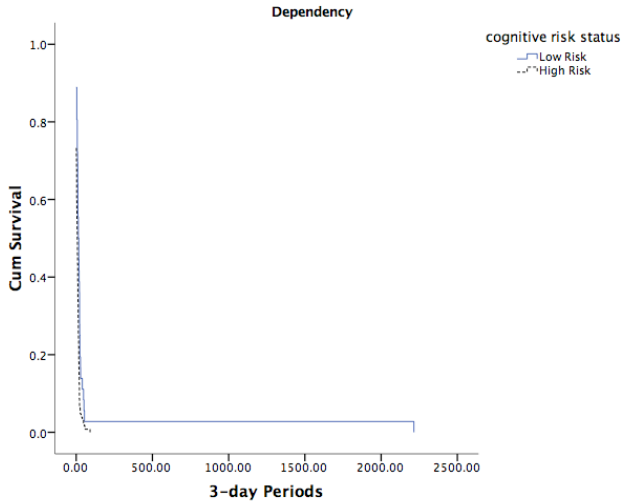
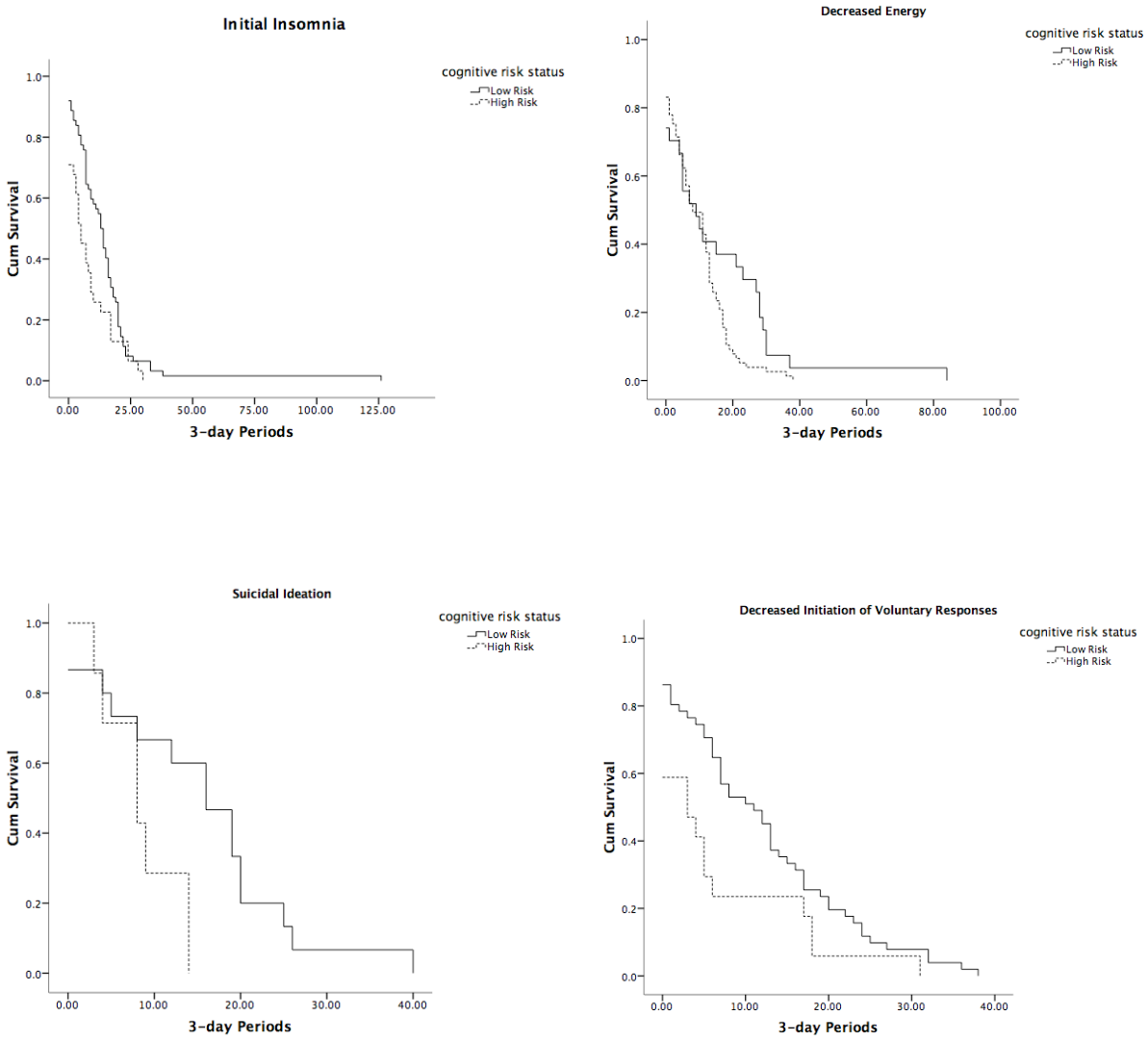


Figure 9. Survival Curves for Time Between Symptom Offset and End of Remission in HR and LR Participants.



Hypothesis 8:

There were 43 episodes that qualified for a diagnosis of endogenous depression. Survival analyses of each symptom experienced in these episodes yielded probability densities (risk of onset) for each 3-day period from the onset of the prodromal period, which were then graphed to display the likelihood of the symptom occurring over time. Figure 10 presents the probability density functions for the onset of each symptom experienced in an endogenous depression.

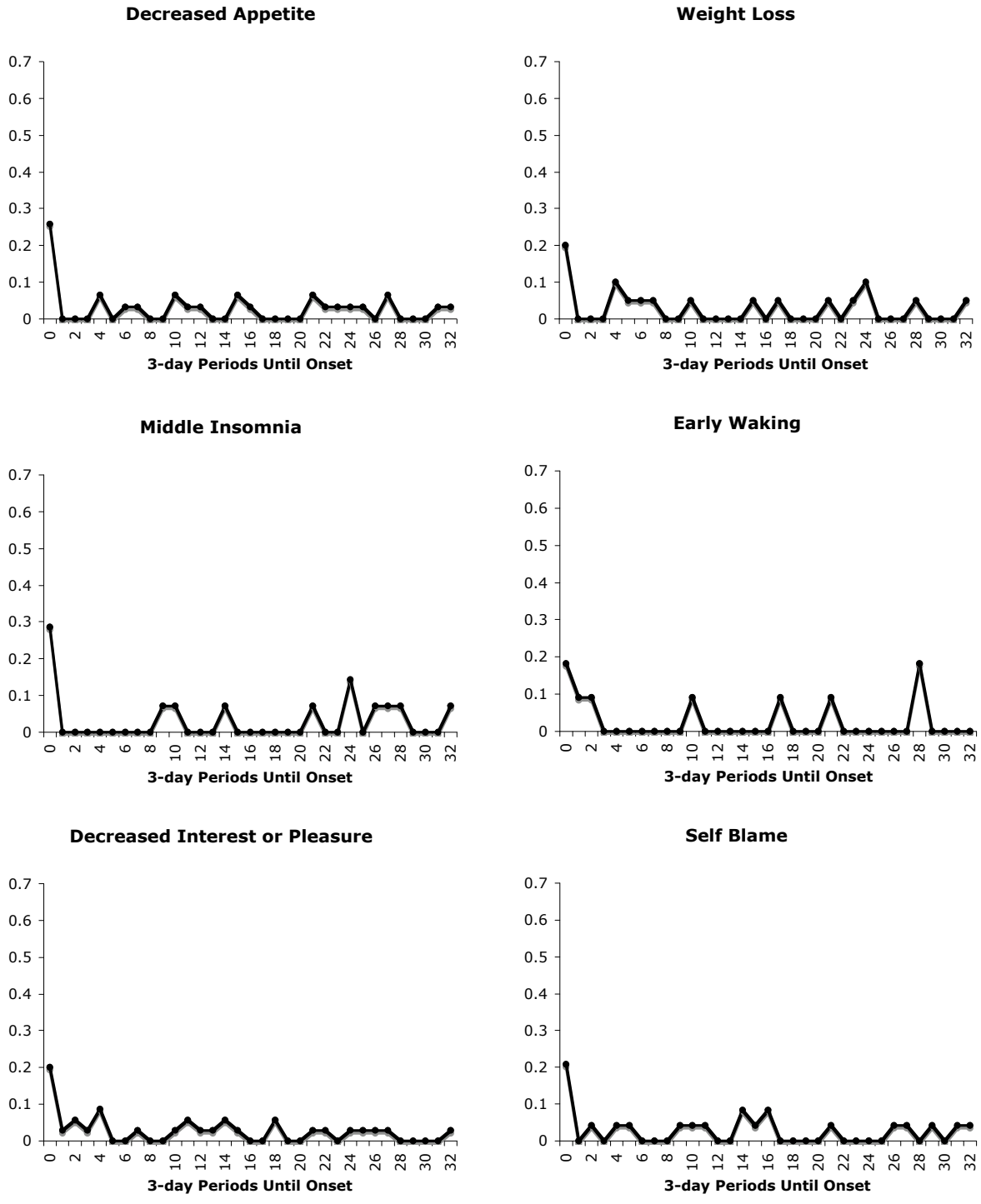
Visual inspection of the graphs indicates that the symptom of hopelessness appeared to have the most drastically declining probability density function of all the symptoms assessed. Decreased appetite, decreased interest or pleasure, sad mood, increased appetite, weight gain, decreased self-esteem and decreased initiation of voluntary responses had initially high and generally declining probability densities as well. Inability to cry and somatic complaints appeared to have initially low probability densities that later peaked. Linear and relatively constant probability density rates were observed for the other symptoms.

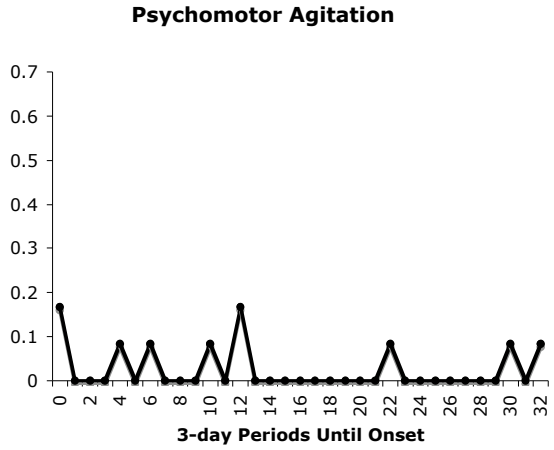
Hypothesis 9:

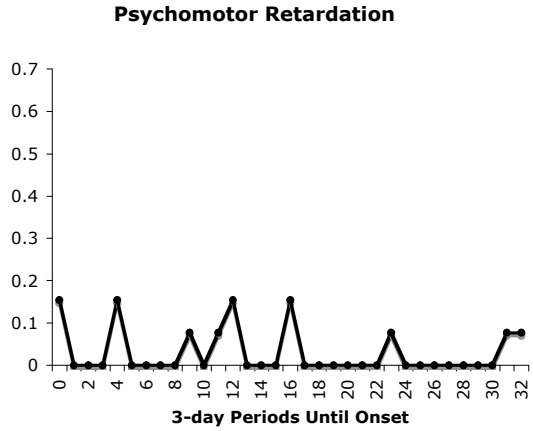
Figure 11 presents the graphs of the probability density functions for the time between symptom offset and the end of the remission phase for symptoms experienced in endogenous depressions. Visual inspection of the graphs indicates that the symptoms of hopelessness and decreased self-esteem appeared to have the most drastically declining probability density functions of all the symptoms assessed. The functions for sad mood, early waking, decreased interest or pleasure, somatic complaints, dependency and decreased initiation of voluntary responses had initially high and generally declining probability densities as well. The other symptoms had generally linear and relatively constant probability density graphs.

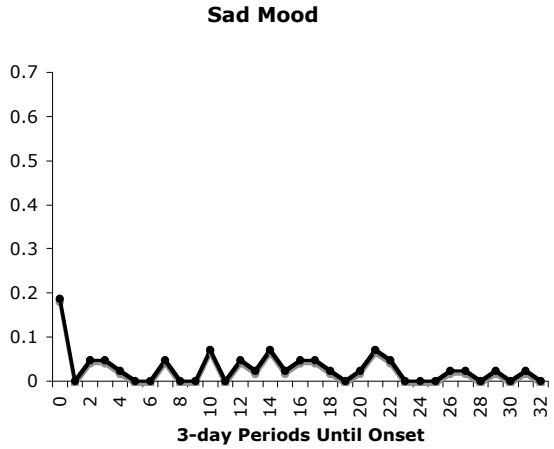
Figure 10. Probability Density Functions for Symptom Onset in Endogenous Depressions.

Endogenous Depression Symptoms:

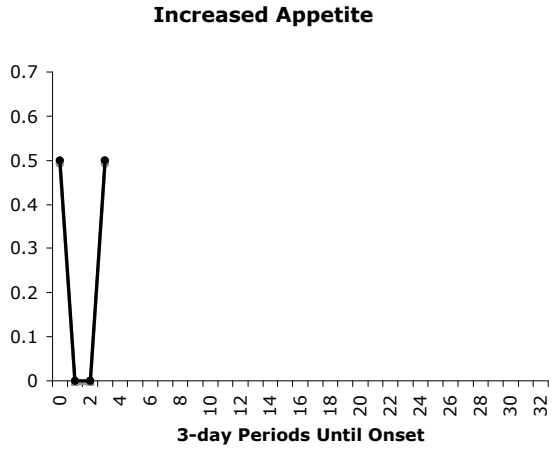


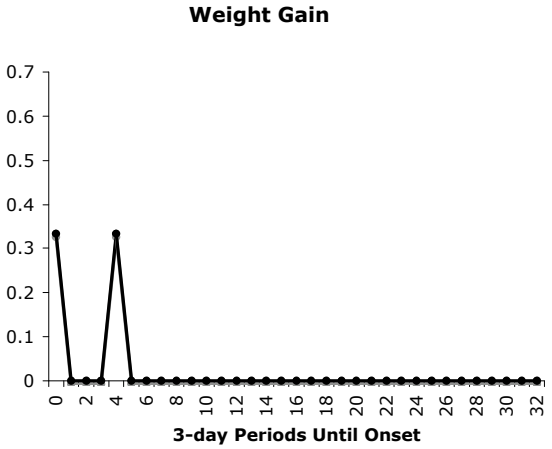


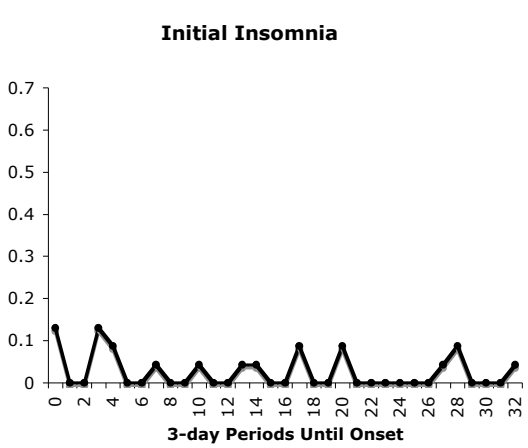




Other Symptoms:






Initial Insomnia
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0.6
0.5
0.4
0.3
0.2
0.1
0
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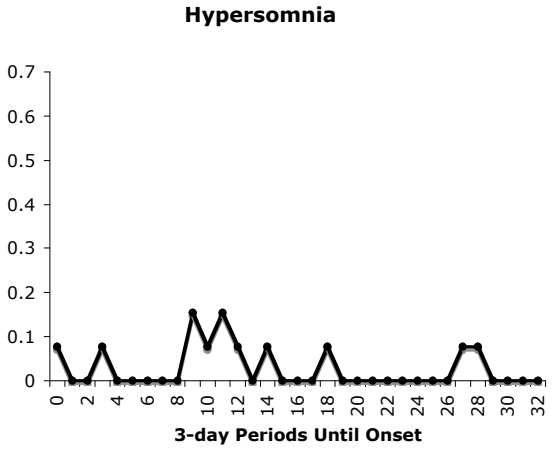
3-day Periods Until Onset


Hypersomnia
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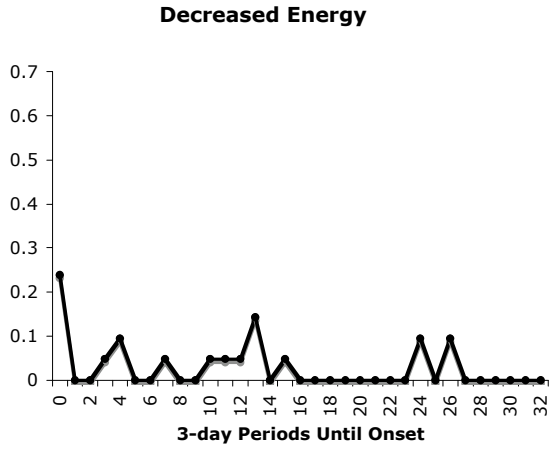
0.6
0.5
0.4
0.3
0.2
0.1
0
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32
3-day Periods Until Onset


Decreased Energy
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0.2
0.1
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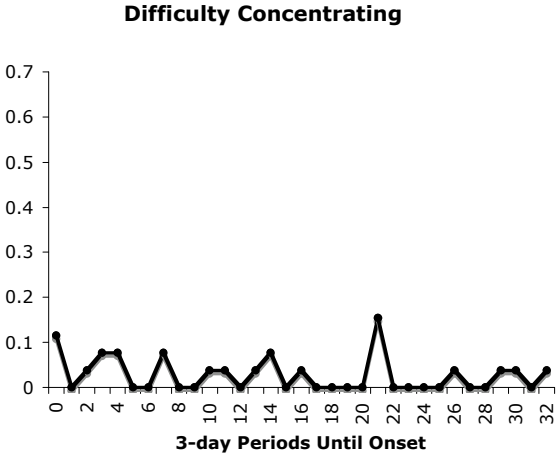
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32
3-day Periods Until Onset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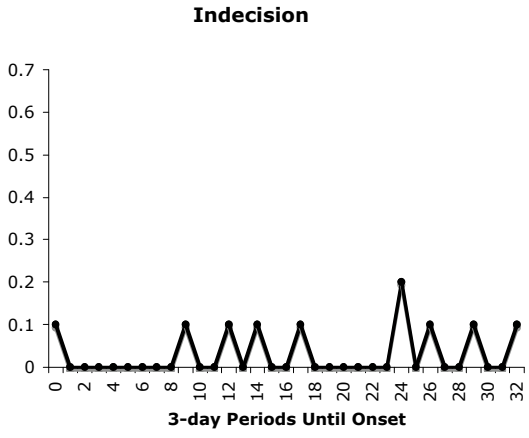
0
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32
3-day Periods Until Onset


Indecision
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0.1
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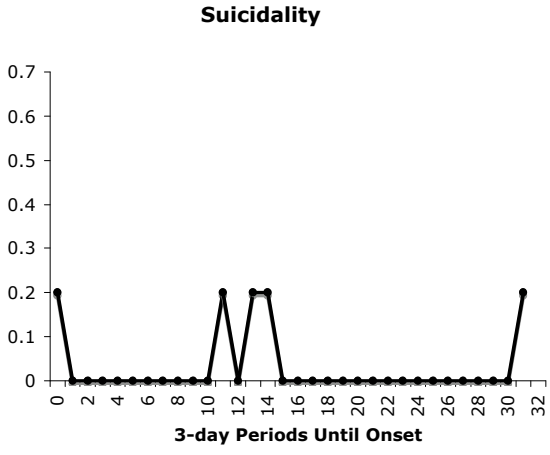
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32
3-day Periods Until Onset


Suicidality
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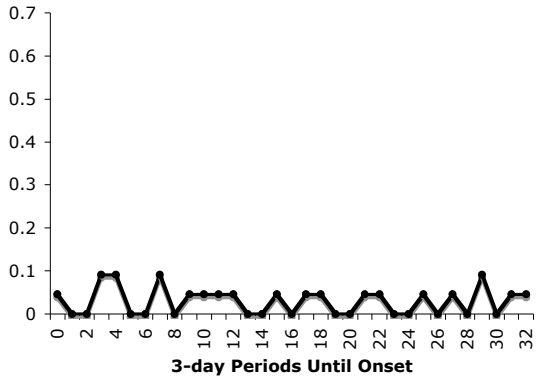
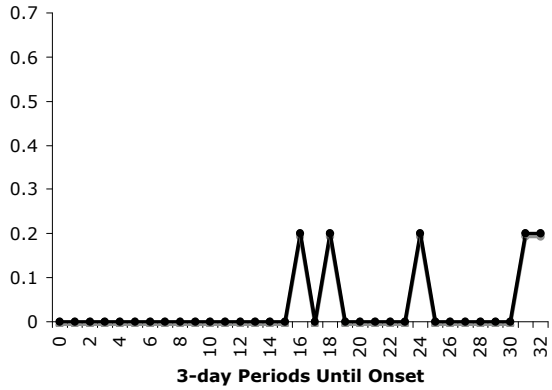
0
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32
3-day Periods Until Onset

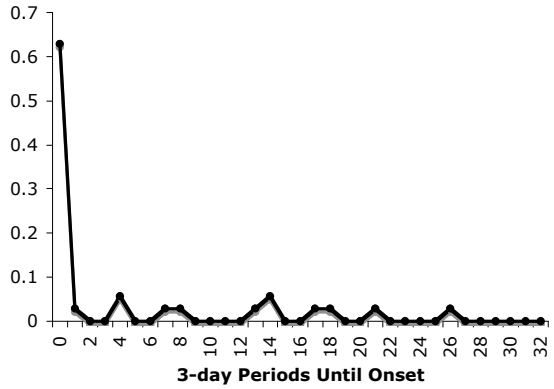
Crying



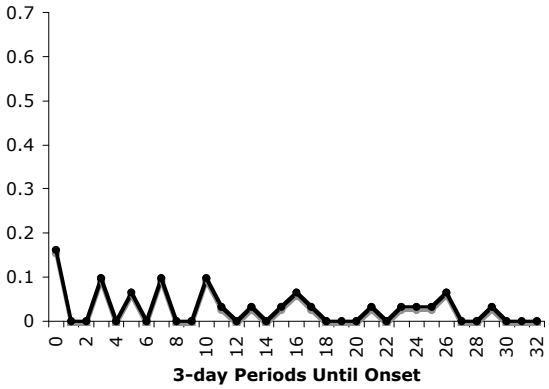
Inability to Cry



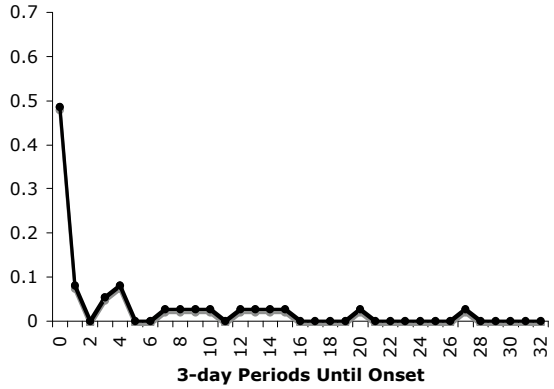
Hopelessness



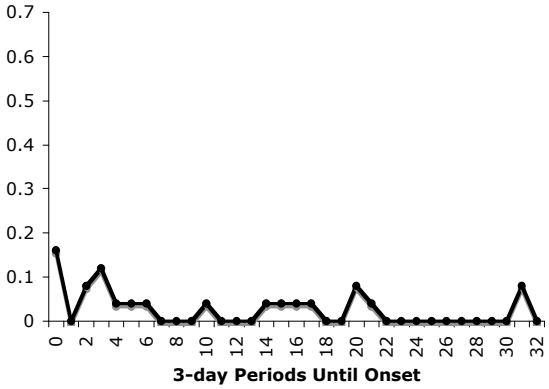
Brooding / Worry



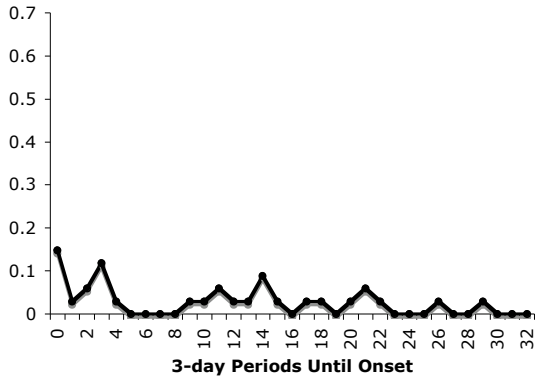
Decreased Self-Esteem



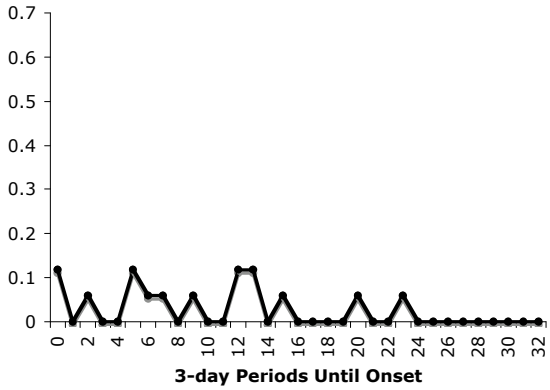
Irritability



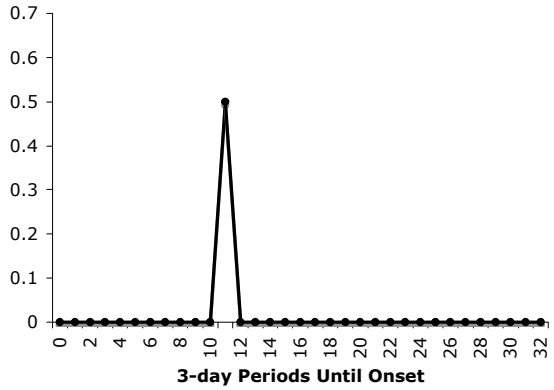
Dependency



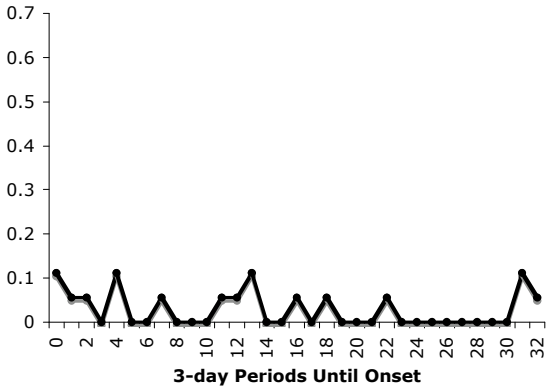
Self-Pity



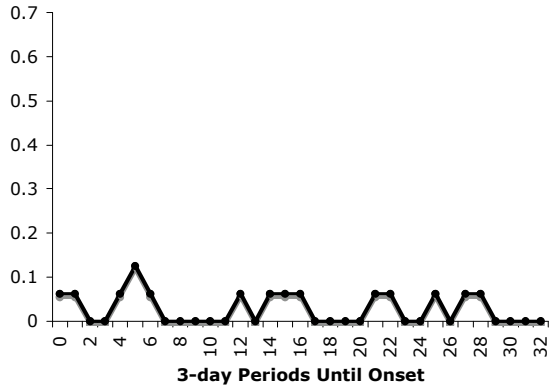
Somatic Complaints



Decreased Effectiveness



Helplessness



Decreased Initiation of Voluntary Responses

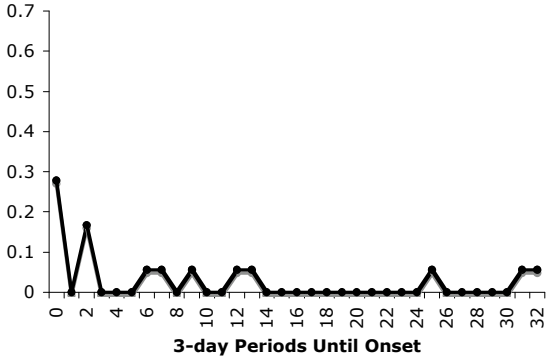
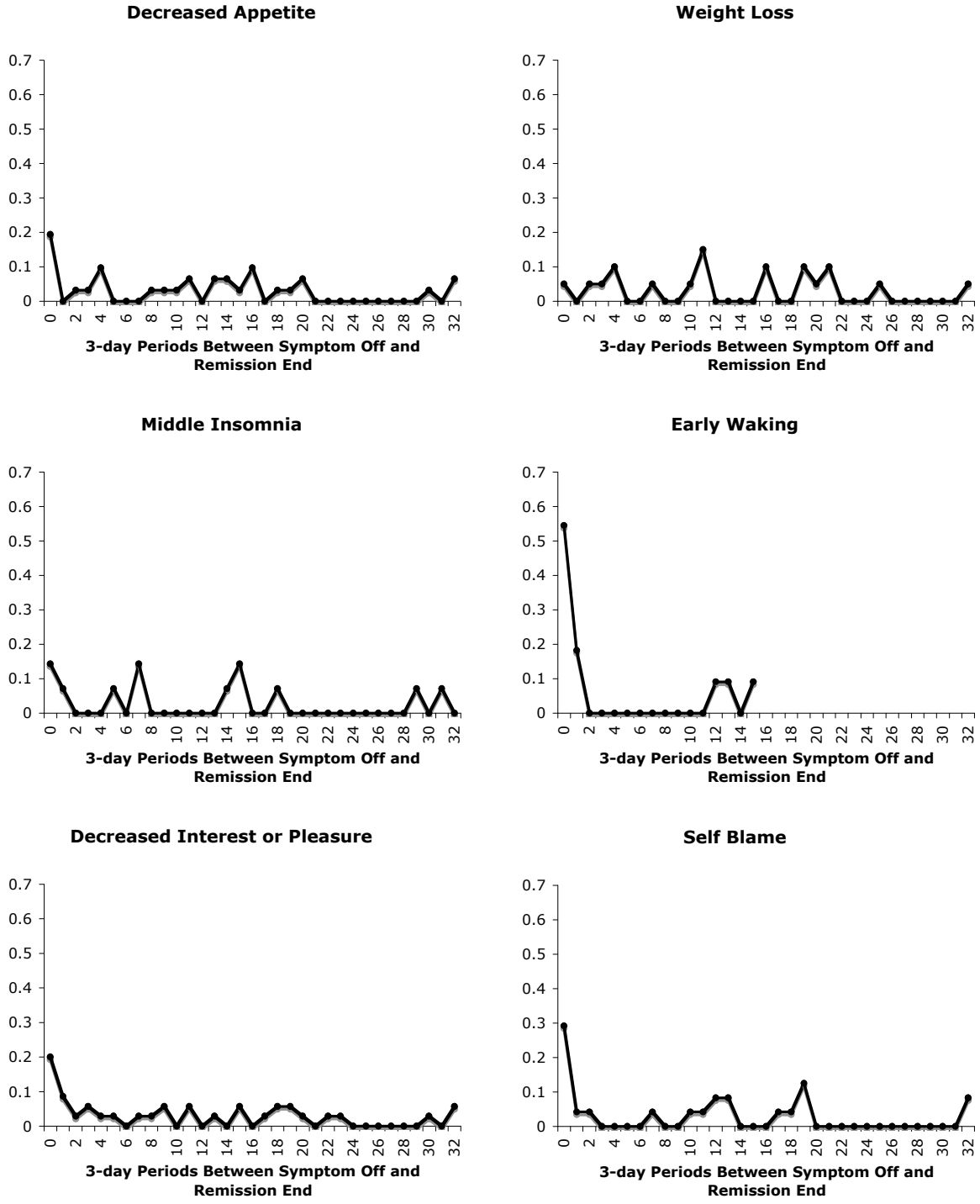
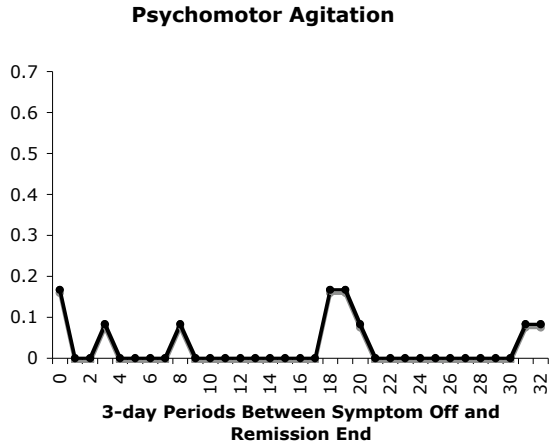
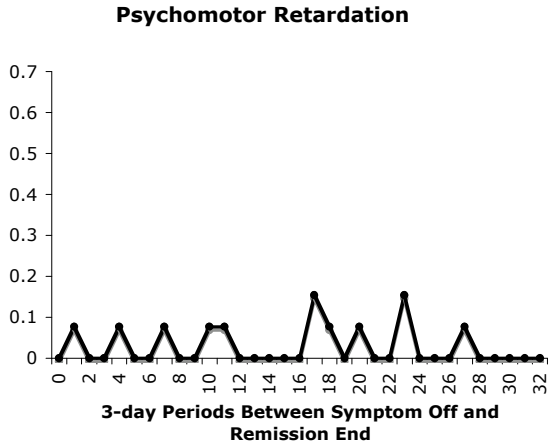


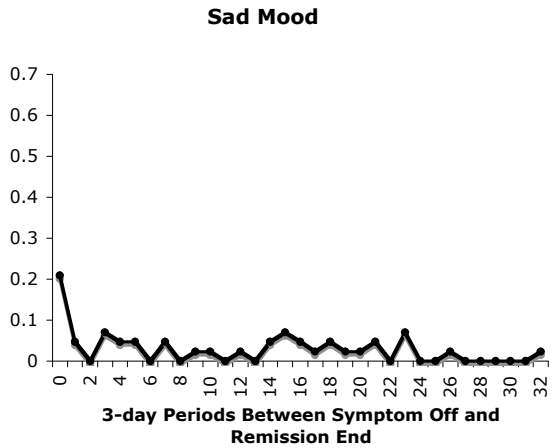
Figure 11. Probability Density Functions for Symptom Offset in Endogenous Depressions.

Endogenous Depression Symptoms:

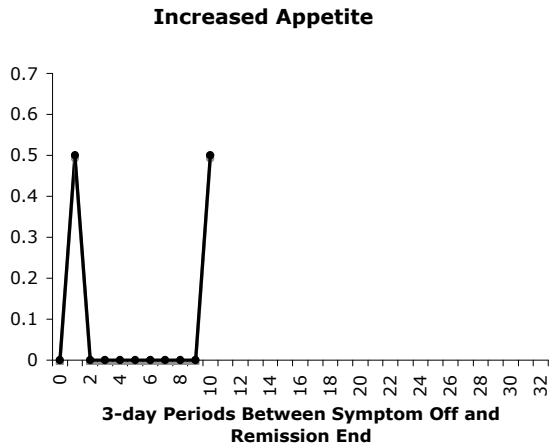


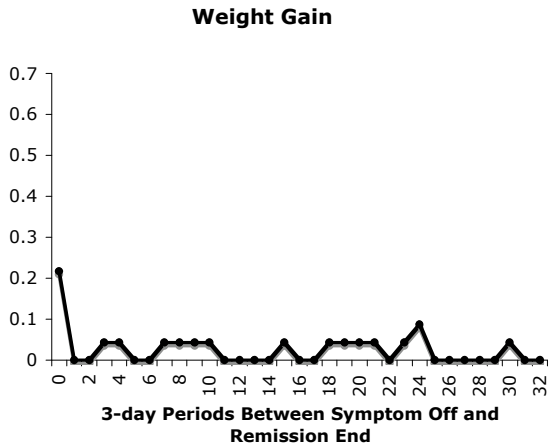




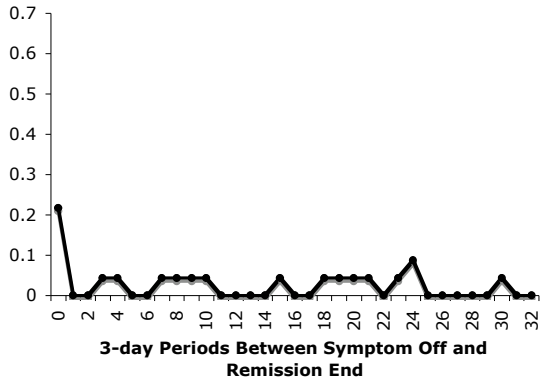


Other Symptoms:

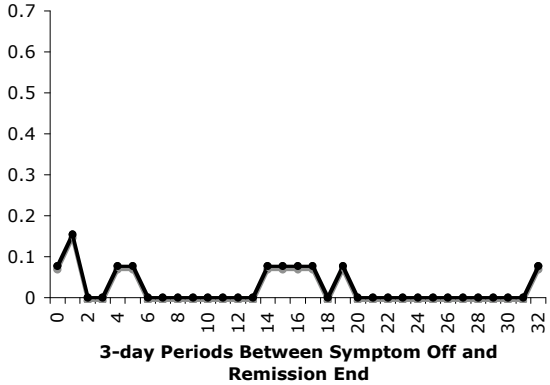




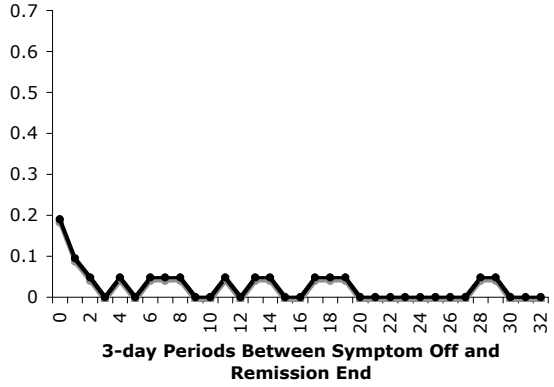
Initial Insomnia



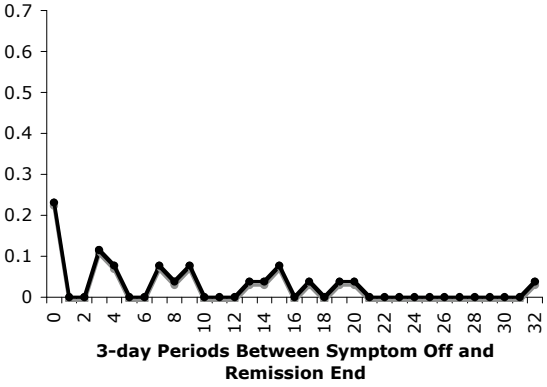
Hypersomnia



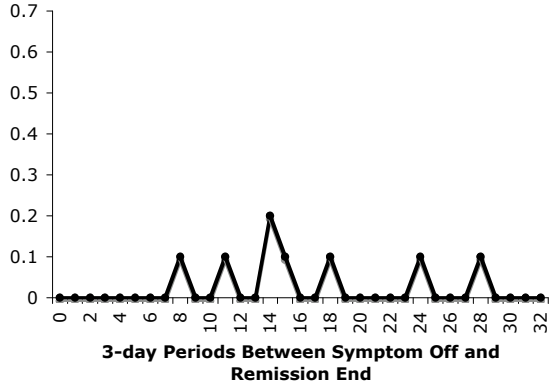
Decreased Energy



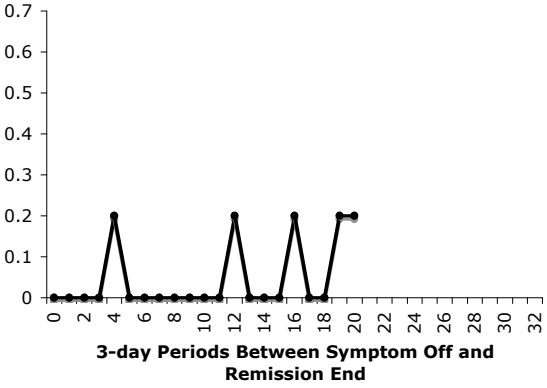
Difficulty Concentrating



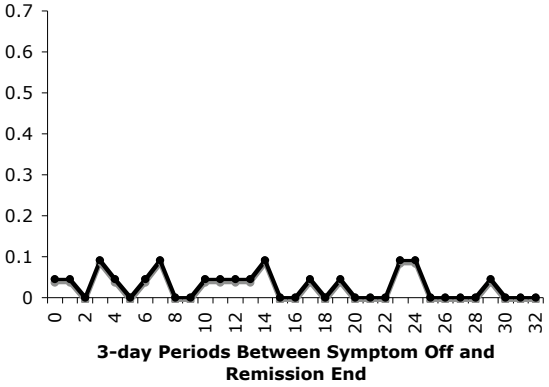
Indecision



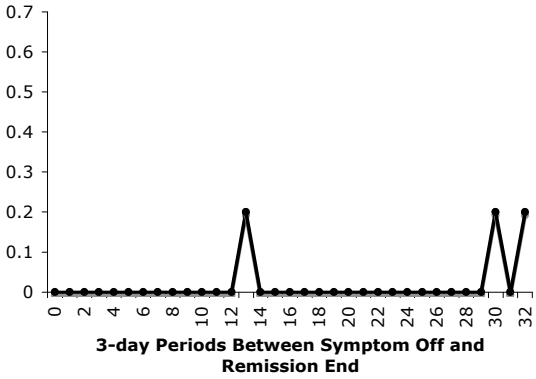
Suicidality



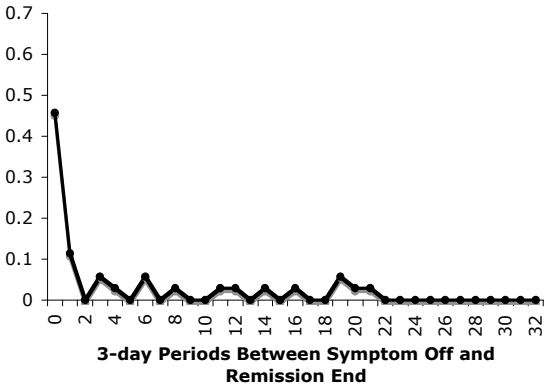
Crying



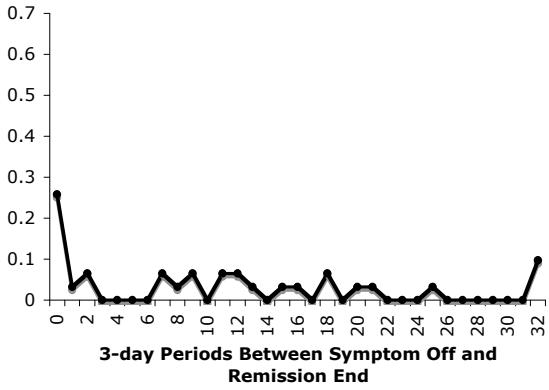
Inability to Cry



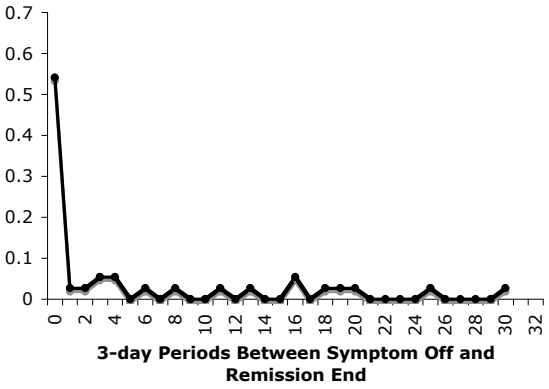
Hopelessness



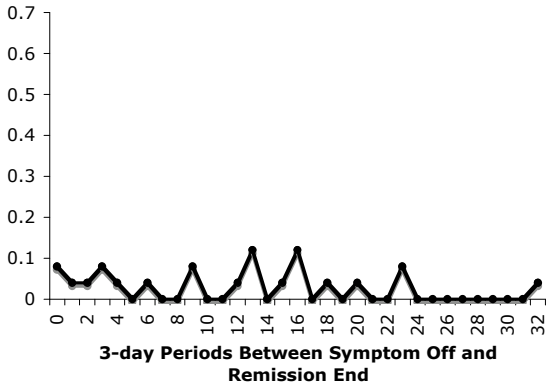
Brooding / Worry



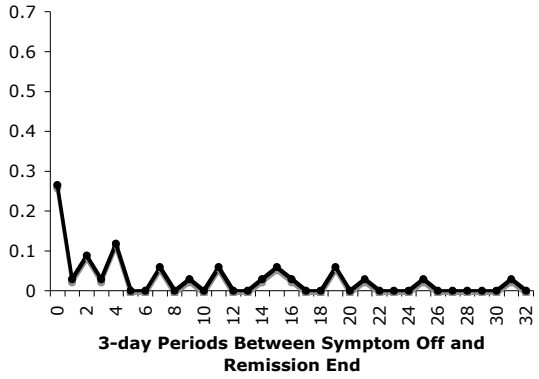
Decreased Self-Esteem



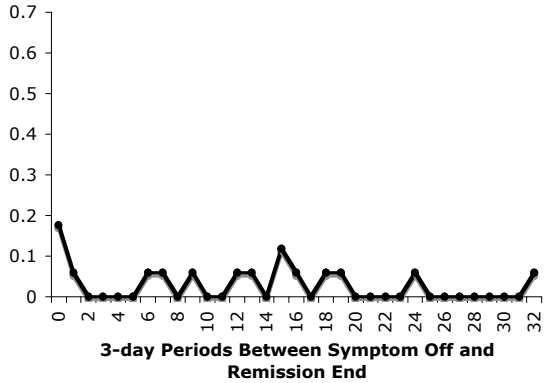
Irritability



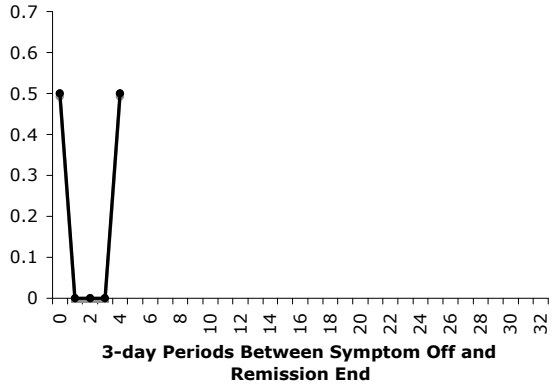
Dependency



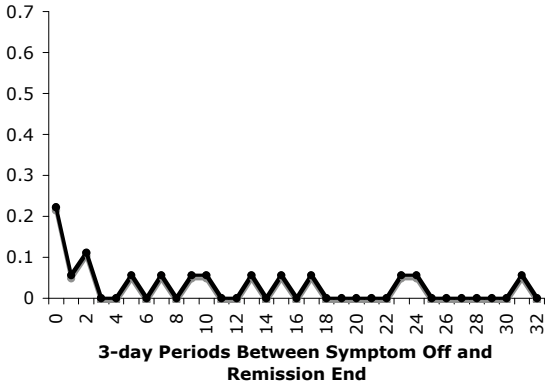
Self-Pity



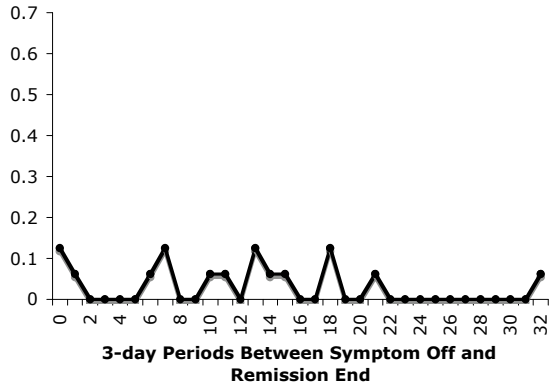
Somatic Complaints



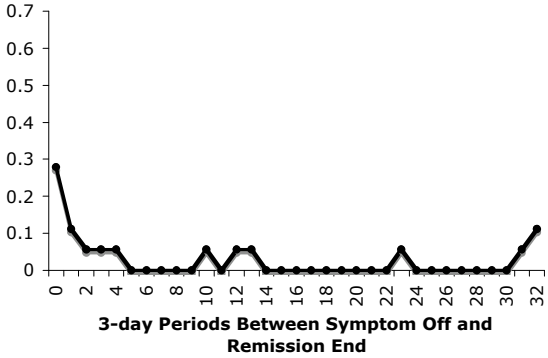
Decreased Effectiveness



Helplessness



Decreased Initiation of Voluntary Responses



Hypothesis 10:

Survival analyses were conducted on each symptom's time to onset (in 3-day intervals) and survival curves compared across high- and low-sociotropy groups. Log-rank analyses suggested significantly different survival curves for the onset of decreased interest or pleasure ($\chi^2(1) = 7.072$ p=.008), crying more ($\chi^2(1) = 7.125$, p= .008), irritability ($\chi^2(1) = 3.974$, p= .046) and self-pity ($\chi^2(1) = 8.079$, p= .004). For each of these symptoms, the HS group demonstrated a significantly shorter survival to symptom onset than the LS group, indicating that these symptoms appear earlier for the HS participants. Figure 12 displays the survival curves for each group for each of these symptoms. No other symptoms were found to have statistically different survival curves for symptom onset.

Hypothesis 11:

Survival analyses were conducted on each symptom's time between offset and end of the remission phase (in 3-day periods) and survival curves compared across high- and low-sociotropy groups. Log-rank analyses suggested significantly different survival curves for the offset of initial insomnia ($\chi^2(1) = 6.909$, p= .009), decreased interest or pleasure ($\chi^2(1) = 5.707$, p= .017), self-blame ($\chi^2(1) = 9.615$, p=.002), crying more ($\chi^2(1) = 3.967$, p= .046), self-pity ($\chi^2(1) = 3.924$, p=.048) and decreased effectiveness ($\chi^2(1) = 6.273$, p=.012). For each of these symptoms, the HS group demonstrated a significantly shorter survival time between symptom remission and the remission of the very last symptom as compared to the LS group. This indicates that these symptoms remit later, remaining closer to the end of the remission phase, for the HS participants. Figure 13 displays the survival curves for each group for each of these symptoms. No other symptoms were found to have statistically different survival curves for the time between symptom offset and the end of the remission phase.

Figure 12. Survival Curves for Time to Symptom Onset in HS and LS Participants.

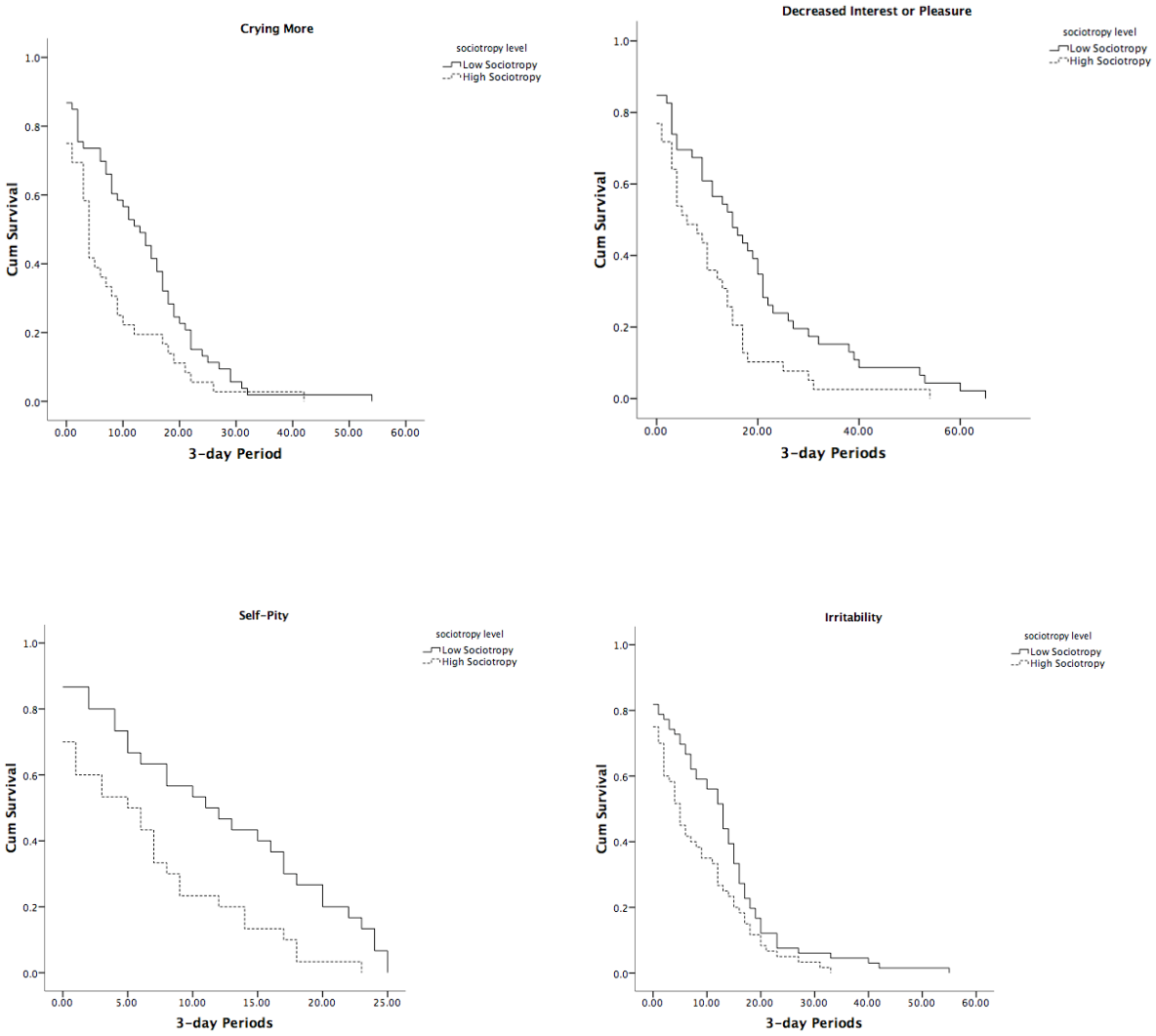
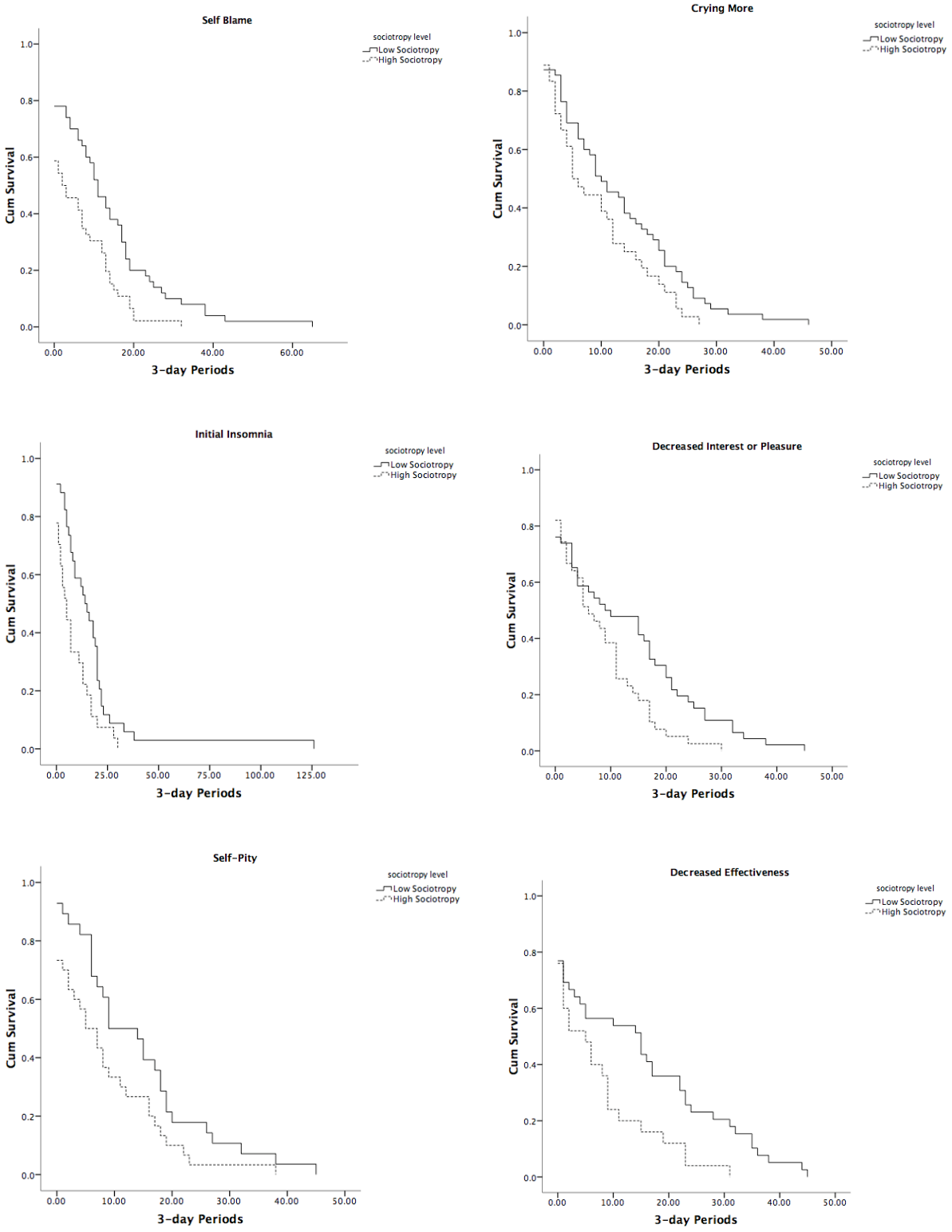


Figure 13. Survival Curves for Time Between Symptom Offset and End of Remission in HS and LS Participants.



Hypothesis 12:

Survival analyses were conducted on each symptom's time to onset (in 3-day intervals) and survival curves compared across high- and low-autonomy groups. Log-rank analyses suggested significantly different survival curves for the onset of irritability ($\chi^2(1) = 6.138$ p=.013), difficulty concentrating ($\chi^2(1) = 8.173$, p= .004), hypersomnia ($\chi^2(1) = 7.800$, p= .005) and helplessness ($\chi^2(1) = 5.112$, p= .024). Figure 14 displays the survival curves for each group for each of these symptoms. For each of these symptoms, the HA group demonstrated a significantly shorter survival to symptom onset than the LA group, indicating that these symptoms appear earlier for the HA participants. No other symptoms were found to have statistically different survival curves for symptom onset.

Hypothesis 13:

Survival analyses were conducted on each symptom's time between offset and end of the remission phase (in 3-day periods) and survival curves compared across high- and low-autonomy groups. Log-rank analyses suggested significantly different survival curves for the offset of irritability ($\chi^2(1) = 7.001$, p= .008) and difficulty concentrating ($\chi^2(1) = 8.995$, p=.003). For each of these symptoms, the HA group demonstrated a significantly shorter survival time between symptom remission and the remission of the very last symptom as compared to the LA group. This indicates that these symptoms remit later, remaining closer to the end of the remission phase, for the HA participants. Figure 15 displays the survival curves for each group for each of these symptoms. No other symptoms were found to have statistically different survival curves for the time between symptom offset and the end of the remission phase.

Figure 14. Survival Curves for Time to Symptom Onset in HA and LA Participants.

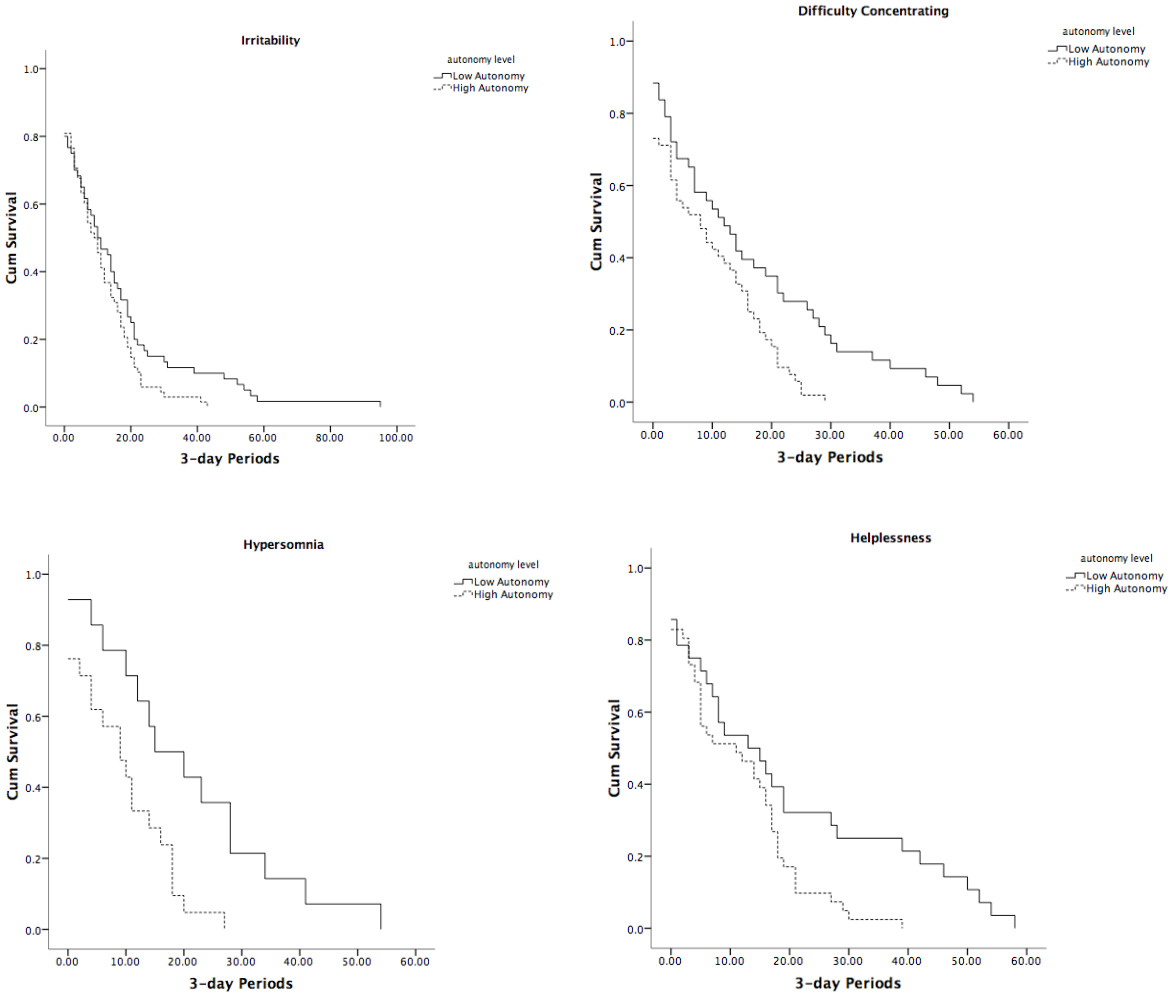
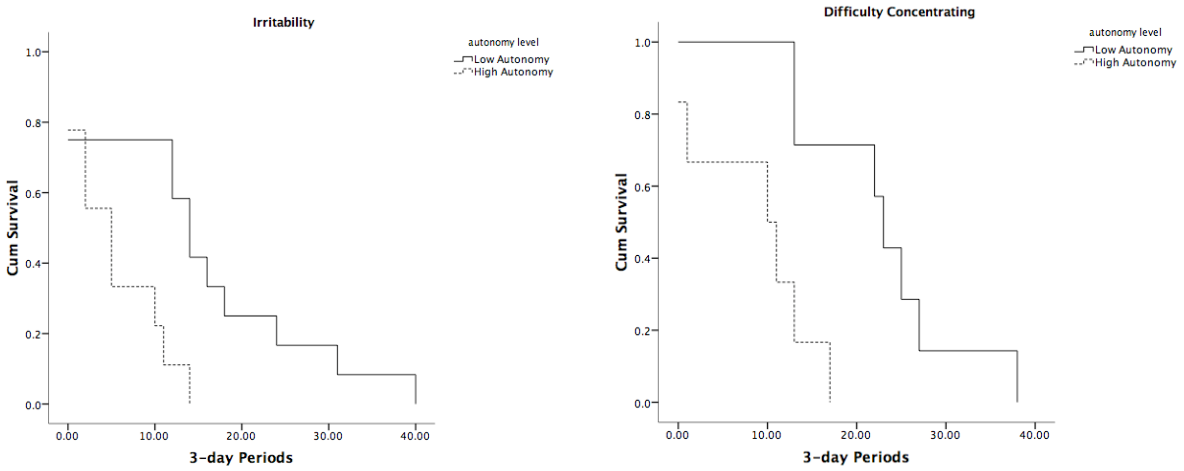


Figure 15. Survival Curves for Time Between Symptom Offset and End of Remission in HA and LA Participants.



CHAPTER 4
DISCUSSION

This study provided an opportunity to examine the early course of depression by testing a conceptual model for the development and remission of depressive symptoms. In this model, prodromal symptoms emanate from the core pathological processes underlying the disorder and comprise the core syndrome as the earliest symptoms to appear, with episodes of depression representing the more pronounced peaks of symptomatology; in this model, these core symptoms would also be the last to remit. Several general hypotheses generated from this model were tested. Additionally, the hopelessness and endogenous subtypes of depression were conceptualized within this model and examined, in an effort to support the applicability of the model. The cognitive personality modes of sociotropy and autonomy were also examined as predictors of specific prodromal and residual symptoms.

Although prior studies provided early evidence for the existence of a prodromal phase and specific symptoms that were more likely to be observed in individuals who would go on to develop a depressive episode than those who would not (see Jackson, Cavanaugh & Scott, 2003 for a review), most were based on small samples and retrospective reports. The current study overcame these methodological limitations, as it was a longitudinal, prospective study that utilized sensitive, semi-structured interviews administered by trained and experienced interviewers in a large sample. An important preliminary finding of this study was that there does appear to be a discernable prodromal phase to depressive episodes, as well as several symptoms that appear to be common to the depressive prodrome across individuals. The finding that there is a period of subsyndromal symptomatology preceding and leading into a depressive episode is an important one. Indicators from this prodromal phase could highlight the expected course of the depressive episode, including the order of symptom offset and the duration of the remission phase. Moreover, the specific symptoms experienced in the prodrome could highlight some of

the processes underlying the depression. All of these are important pieces of information for treatment providers. Thus, this phase of the depressive experience is ripe for further study.

Subsyndromal depressive symptoms are not uncommon experiences for many individuals (e.g., Judd, Akiskal & Paulus, 1997), even those who do not go on to experience an acute episode of depression. This study provided an opportunity to explore which symptoms of depression were more likely to be present in the prodromal phase of an acute episode than in the normal experience of depressive symptoms that any individual could be expected to encounter. Such symptoms may be important to explore as indicators of an impending episode of depression. Indeed, the current study identified nine symptoms that were more likely to be present among individuals entering a depressive episode than individuals matched on age, gender, ethnicity and cognitive risk status. These include sad mood, decreased interest in or pleasure from activities, self-blame, difficulty concentrating, hopelessness, worrying/brooding, decreased self-esteem, irritability and increased dependency. These symptoms appear to be related to the prodromal phase and thus could represent early warning signs that an individual could be developing an acute episode of depression. It is important to note that individual differences in symptom presentation exist, as evidenced by tests of the other hypotheses in this study, and, thus, the appearance of these symptoms will not always indicate that an episode of depression is forthcoming. Certainly, there is a risk in overpathologizing the presentation of prodromal symptoms. Sometimes isolated depressive symptoms do exist. It is thus important for individuals, as well as their treatment providers, to be mindful of the specific symptoms that are salient to them, across episodes of depression, before ascribing too much importance to the emergence of specific symptoms of depression.

General Hypotheses:

Four general hypotheses were tested from the conceptual model hypothesized in this study. The first, that the profiles of the symptoms present in the prodromal and residual phases

would be similar, received substantial support (median κ = .605, mode = 1.0), according to Landis and Koch (1977). These results indicate that those symptoms present during the prodrome of a depressive episode are very similar to those in the residual phase and are typically among the latest symptoms to remit. This provides strong evidence that prodromal symptoms are most likely to remain present throughout the depressive experience, and supports the notion that these "primary" symptoms could represent the core syndrome of the disorder. Other symptoms are experienced more during the acute phase and tend to remit as the acute episode ends. The relation between the primary, core symptoms and the secondary symptoms experienced during an episode of depression remains to be studied. However, the current study provides some support for the hypothesis that there is a difference between these sets of symptoms and that some relation between them exists, given the patterns of temporal onset identified in this study.

The second hypothesis tested, that the durations of prodromal and residual phases would be correlated, was also supported, with a moderate, significant correlation (ρ = .486). Additionally, the order of symptom onset and remission was found to be substantially, negatively correlated (ρ = -.642), indicating that the order of symptom remission was similar to the reverse of the order of onset. The earliest symptoms were among the very last to remit. Taken together, the support for each of these three hypotheses begins to paint a picture of the relation between the earliest and latest, or the prodromal and residual, phases of a depressive episode. The durations of each phase tend to be related, the symptom profile is similar across phases, and the order of symptom onset is related to the reverse order of symptom remission. The earliest symptoms to present appear to be the latest to remit. Thus, the three major hypotheses generated from the conceptual model of the development and remission of the depressive episode were supported in this study.

The fourth general hypothesis, that prodromal symptom profiles would be similar across episodes of depression, was not strongly supported by the analyses conducted in this study (mean

κ = .40). It would appear from these findings that individuals do not demonstrate a great degree of consistency in the earliest symptoms that present across episodes of depression. Similar results were obtained in a study of symptom consistency across episodes, which found that the degree of correlation observed between symptom profiles of subsequent episodes of depression was low; the agreement observed was largely that to be expected by chance (Young, Fogg, Scheftner & Fawcett, 1990). However, Young and colleagues also demonstrated that when the total number of symptoms experienced was taken into account, and episodes are only compared with episodes that include similar numbers of symptoms overall, the concordance of symptom presentation was high. When one episode has many fewer symptoms than the other, the concordance of symptoms appears lowered, and perhaps artificially so. This could also be the case when comparing symptom profiles across prodromal phases. If one prodrome includes three symptoms and the next prodrome includes the same three as well as 4 others, the "hit rate" is only 43%. This low percentage might obscure the fact that all three symptoms experienced in prodrome A were also present in prodrome B. Thus, symptom presentation across prodromes may demonstrate a degree of consistency that is moderated by the intensity of the prodrome. Accordingly, results from these analyses should be interpreted with caution, as the analyses employed herein did not account for prodrome intensity.

The Hopelessness Subtype:

Episodes from the final sample that qualified for the diagnosis of hopelessness depression were subjected to analyses to elucidate patterns of symptom onset and offset. In particular, it was hypothesized that hopelessness would be the first symptom to emerge in these episodes, followed by symptoms such as sad mood, retarded initiation of voluntary responses, suicidality, initial insomnia, decreased energy, self-blame, difficulty concentrating, psychomotor retardation, brooding/worrying, lowered self-esteem and dependency. Secondary symptoms would appear after these core symptoms. Survival analyses of the time between the earliest symptom onset and

each of these symptoms yielded probability density functions, which displayed the probability of the symptom presenting over time. These graphs illustrated patterns insofar as the symptoms with relatively high and rapidly declining probability densities were those that were most likely to have appeared earliest. Graphs that were relatively linear came from symptoms that did not have a particular pattern of early or late symptom onset. Consistent with hypothesis, hopelessness exhibited a pattern of being the earliest symptom to emerge. Moreover, sad mood, self blame, brooding/worry, decreased self-esteem, dependency and decreased appetite had initially high and generally declining probability densities as well. This indicates that these were the symptoms most likely to onset at or near the very beginning of the prodromal phase. Linear and relatively constant probability density rates were observed for the other symptoms. Thus, support for the notion that specific symptoms, directly related to the hopelessness subtype, would be the first to emerge was obtained from these analyses.

The order of symptom remission in hopelessness depressions was also examined. According to the hypothesis, the core symptoms would be the latest to remit, with hopelessness specifically being the latest. Probability density graphs were generated for each symptom, with "time" reflecting the amount of time between the last symptom to remit and the remission of the symptom in question. Essentially, the time in these graphs was in reverse- time 0 represents the last symptom to remit, longer times represent symptoms that remitted much earlier than the last symptom. This was done to standardize the endpoint of all episodes and to generate graphs that could be easily compared to the graphs for symptom onset. The probability density graphs for symptom remission indicated that hopelessness and decreased self-esteem appeared to have the most drastically declining probability density functions of all the symptoms assessed. The functions for sad mood, self blame, brooding/worry, dependency and increased appetite had initially high and generally declining probability densities as well. This indicates that those symptoms were most likely to remit at or near the very end of the remission phase. The other

symptoms had generally linear and relatively constant probability density graphs, indicating that they did not have a particular pattern to their remission.

Thus, the results for symptom onset and remission suggest that hopelessness was typically the earliest symptom to emerge in hopelessness depressions, followed by the core symptoms of sad mood, self blame, brooding/worry, decreased self-esteem and dependency. These were also generally the latest symptoms to remit, with hopelessness and decreased self-esteem typically remitting near the very end. Table 2 summarizes this pattern of results. This supports the notion that the core symptoms are the earliest to present, the latest to remit, and represent the core syndrome of the episode in hopelessness depressions. This pattern could hold for other subtypes, and was tested in the endogenous subtype of depression as well as among individuals at high versus low levels of sociotropy and autonomy.

The Role of Cognitive Risk Status in Symptom Presentation:

Analyses were conducted comparing HR and LR groups on the survival time to symptom onset and the time between symptom remission and the end of the remission phase. HR individuals were hypothesized to be more likely to experience hopelessness depressions (and by extension, the symptoms therein) than LR individuals. This study sought to explore whether these hopelessness depression symptoms would present earlier and remit later in the depressive experience for HR individuals compared to LR individuals. These analyses for symptom onset yielded significant differences between groups for the onset of concentration difficulties, decreased self-esteem and dependency. Survival analyses comparing the survival time between remission of symptoms and the end of the acute phase between HR and LR groups also suggested that only a subset of the hopelessness depression symptoms demonstrated differential patterns. Initial insomnia, decreased energy, suicidal ideation and decreased initiation of voluntary responses were more likely to remit later among the HR than LR participants.

Table 2.

Summary of Probability Density Functions for Symptom Onset and Remission in Hopelessness Depressions

	Onset- High Risk of Early Presentation	Remission- High Risk of Late Remission
Hopelessness Symptoms		
Sad Mood	X	X
Initial Insomnia		
Decreased Energy		
Self Blame	X	X
Difficulty Concentrating		
Suicidality		
Psychomotor Retardation		
Hopelessness	X	X
Brooding/Worry	X	X
Decreased Self-Esteem	X	X
Dependency	X	X
Decreased Initiation of Voluntary Responses		
Other Symptoms		
Decreased Appetite	X	
Weight Loss		
Increased Appetite		X
Weight Gain		
Middle Insomnia		
Early Waking		
Hypersomnia		
Decreased Interest or Pleasure		
Indecision		
Psychomotor Agitation		
Crying		
Inability to Cry		
Irritability		
Self-Pity		
Somatic Complaints		
Decreased Effectiveness		
Helplessness		

The symptoms identified in these analyses as more likely to present earlier and remit later among HR than LR participants were all specifically hypothesized to be associated with hopelessness depression. Thus, the notion that cognitive predispositions can influence the presentation of specific prodromal and residual symptoms was supported. This suggests that an individual's cognitive risk status can impact the trajectory for an episode of depression, with HR individuals experiencing hopelessness depression symptoms earlier than other, secondary symptoms, and having hopelessness depression symptoms be the latest to remit. Studies have demonstrated that a cognitively high-risk individual is at greater risk for developing depression and the subtype of hopelessness depression (Alloy et al., 2006), and this cognitive vulnerability predicts episodes that are more severe and tend not to fully remit between episodes (Iacoviello et al., 2006). Numerous studies have also demonstrated that cognitive vulnerability and hopelessness predict HD symptoms better than non-HD symptoms (e.g., Alloy, Just & Panzarella, 1997; Alloy & Clements, 1998; Abela & D'Alessandro, 2001; Abela, Gagnon & Auerbach, 2007). The current study suggests that cognitive vulnerability also appears to predict the specific prodromal and residual symptoms that an individual might be expected to experience: specifically, the prodromal hopelessness depression symptoms of concentration difficulties, decreased self-esteem and dependency and residual hopelessness depression symptoms of initial insomnia, decreased energy, suicidal ideation and decreased initiation of voluntary responses. It is noteworthy that, according to the present analyses, HR individuals do not appear to develop hopelessness earlier than LR individuals. The symptom of hopelessness, when present in an episode of depression, tends to appear early in the process regardless of cognitive risk status.

The Endogenous Subtype:

Table 3 summarizes the results from the probability density graphs generated from survival analyses of symptoms experienced in episodes that met criteria for endogenous depression. In these episodes, hopelessness appeared to have the most drastically declining

Table 3.

Summary of Probability Density Functions for Symptom Onset and Remission in Endogenous Depressions

	Onset- High Initial, Generally Declining Risk	Remission- High Risk of Late Remission
Endogenous Symptoms		
Decreased Appetite	X	
Weight Loss		
Middle Insomnia		
Early Waking		X
Decreased Interest or Pleasure	X	X
Self Blame		
Psychomotor Agitation		
Psychomotor Retardation		
Sad Mood	X	X
Other Symptoms		
Increased Appetite	X	
Weight Gain	X	
Initial Insomnia		
Hypersomnia		
Decreased Energy		
Difficulty Concentrating		
Indecision		
Suicidality		
Crying		
Inability to Cry		
Hopelessness	X	X
Brooding/Worry		
Decreased Self-Esteem	X	X
Irritability		
Dependency		X
Self-Pity		
Somatic Complaints		X
Decreased Effectiveness		
Helplessness		
Decreased Initiation of Voluntary Responses	X	X

probability density function of all the symptoms assessed. Decreased appetite, decreased interest or pleasure, sad mood, increased appetite, weight gain, decreased self-esteem and decreased initiation of voluntary responses had initially high and generally declining probability densities as well. This indicates that these were the symptoms most likely to onset at or near the very beginning of the prodromal phase.

As for symptom remission, hopelessness and decreased self-esteem appeared to have the most drastically declining probability density functions of all the symptoms assessed. The functions for sad mood, early waking, decreased interest or pleasure, somatic complaints, dependency and decreased initiation of voluntary responses had initially high and generally declining probability densities as well. This indicates that those symptoms were most likely to remit at or near the very end of the remission phase. Taken together, there appears to be some consistency among the symptoms earliest to present and latest to remit in endogenous depressions, as Table 3 indicates five of the eight symptoms commonly experienced in each of these phases of endogenous depressions overlapped. This further supports the general model tested in this study, whereby the earliest symptoms to present are the latest to remit. However, these symptoms were not specific to the endogenous subtype; only decreased interest or pleasure and sad mood were the symptoms hypothesized to be associated with endogenous depression that were consistently present in the prodromal and remission phases.

Symptom Patterns Among High- versus Low-Sociotriopy and Autonomy Individuals:

Survival analyses comparing the survival time to symptom onset between HS and LS groups suggested significantly different survival curves for the onset of five specific symptoms: decreased interest or pleasure, crying more, irritability and self-pity. Analyses also suggested significantly different survival curves for the time-to-remission of decreased interest or pleasure, crying more, self-pity, initial insomnia, self-blame and decreased effectiveness. So a pattern of decreased interest or pleasure, crying more and self-pity tending to appear earlier and remit later

among HS than LS individuals emerges from these data. This suggests a role of sociotropy in the presentation and remission of these symptoms. These results suggest that highly sociotropic individuals, as they become depressed, tend toward an early pattern of feeling very badly for themselves, feeling less pleasure in their lives and possibly withdrawing from activities that might bring them pleasure, and crying more. These symptoms remain towards the end of their depressions as well, more so than for LS individuals. This supports the hypothesis that sociotropy, as a cognitive-personality characteristic, can influence the presentation of specific symptoms of depression; here seen as decreased interest or pleasure, crying more and self-pity. It is important to note that, besides crying more, these symptoms are not among those empirically demonstrated to be associated with sociotropy (Robins et al., 1989; 1995; 1997). Still, they do correspond with the "core sense of deprivation… such as thoughts of loss, feeling lonely and unlikable, and crying" experienced by the depressed, sociotropic individual hypothesized by Beck (1983) and Robins and Luten (1991). That these symptoms are not only characteristic of the nature of a depressed, highly sociotropic individual, but are demonstrated to appear earliest and remit latest, lends credence to the notion that this represents the core of the depressive experience for this group of individuals.

Survival analyses comparing the survival time to symptom onset between HA and LA groups demonstrated significantly different survival curves for the onset of four symptoms: irritability, difficulty concentrating, hypersomnia and helplessness. The groups were also observed to have significantly different survival curves for time-to-remission of two symptoms, irritability and difficulty concentrating. So, a pattern of these two symptoms, irritability and difficulty concentrating, emerging earlier and remitting later among HA than LA individuals surfaces from these data. This might suggest a role of autonomy in the early presentation and later remission of these symptoms, consistent with the general model. However, irritability is the only one of these that has been empirically associated with measures of autonomy in the literature

(Robins et al., 1989; 1995; 1997). Moreover, the other symptoms that have been associated with autonomy, such as hopelessness, decreased interest or pleasure in people or activities/anhedonia, being critical of others, thoughts of death/dying, and suicidal ideation, were not observed to demonstrate the hypothesized pattern of earlier onset and later remission. One reason for this could be found in recent critiques of the scale used to measure autonomy in this study. The autonomy scale of the SAS has been suggested to subsume several potentially diverse factors, including Sensitivity to Others' Control and Independent Goal Attainment, with factor analysis of these scales providing support for this (Bieling, Beck and Brown, 2000). Further, Iacoviello and colleagues (in press) have demonstrated differential effects of these factors on the long-term course of depression, suggesting that their diverse nature could lead them to impart differential effects on symptom presentation as well. Finally, previous studies of autonomy's association with specific symptoms used the Personal Style Inventory (Robins, Ladd, Welkowitz & Blaney, 1994), not the SAS. The use of the SAS may have hampered the current study's effort to highlight the role of autonomy on specific symptom presentation and remission. Instead, perhaps the factors presumed to underlie this scale on the SAS should be analyzed in the future for their ability to predict more specific sets of symptoms that present earlier and remit later in the course of an episode of depression.

Strengths and Limitations:

This study has several strengths. First, the prospective design enabled the onset and remission of depression symptoms to be chronicled in real time, and not assessed by retrospective report. The prospective design and frequent (every 6 weeks) assessments increased the reliability of the semi-structured interview measures of depression symptoms. Moreover, the broad range of symptoms assessed, and the sensitive nature of the measures, allowed for the study of many potential depressive symptoms at subclinical levels. These are all improvements over the methodologies of previous studies of depressive prodromes. Additionally, the participants in this

study were diverse with respect to socioeconomic status, ethnicity and gender. Despite being selected for the CVD Project based on cognitive risk status, the sample is quite representative of the young adult population and, as such, the findings of this study should be generalizable to this population.

A limitation of the current study was the inclusion of some participants who had a prior history of depression. It would have been ideal to only include individuals with no prior depression, so that the assessment of cognitive risk status, sociotropy and autonomy would be unequivocally devoid of impact from previous depression. Another possible limitation is the measure of autonomy used in this study, the Sociotropy-Autonomy Scale (SAS). The autonomy scale has come under scrutiny of late as it is now assumed to comprise several disparate factors, which could differentially influence symptom presentation. A more valid measure of autonomy such as the Personal Style Inventory, might be used in future studies of autonomy's impact on symptom presentation to overcome this limitation. Finally, the current study was limited in its ability to examine the pattern of symptom onset between the prodromal or primary symptoms and the secondary symptoms to appear in different subtypes of depression. Analyses relied on the visual comparison of probability density graphs to identify symptoms earliest to appear and latest to remit. More accurate analyses should be conducted in future studies where available.

Conclusions:

The current study provided support for several key hypotheses generated from a conceptual model of the development and remission of depressive symptoms. Namely, the duration of the prodromal and residual phases of depressive episodes are significantly correlated. The symptoms to present earliest, during the depressive prodrome, are also likely to remit latest, possibly remaining as residual symptoms. Further, the order of symptom onset is strongly related to the order of symptom offset, in reverse. Taken together, the early (prodromal) and late (remission) phases of a depressive episode have some strong similarities, especially as concerns

the presentation and remission of symptoms. These symptoms that present earliest and remit latest are important insofar as they might be thought to comprise the core syndrome of the depressive episode. Their nature could potentially highlight processes underlying the depression, and they could represent important treatment targets if they are, in fact, the core syndrome of the episode. Future research should investigate further the role of prodromal symptoms in the course of a depressive episode. Moreover, research is warranted into the specific treatment of prodromal symptoms of depression. Such early intervention could help thwart the development of an acute episode of depression. Or, when an acute episode has already developed, understanding the core pathology might help in focusing more effective treatments.

Based on the current study, secondary symptoms are thought to "build off of" the prodromal, core symptoms of a depression, in a process that could be considered akin to dual vulnerabilities. This theory of dual processes, whereby an initial vulnerability triggers a core syndrome or cluster of primary symptoms, which then, in turn, trigger moderating vulnerabilities or otherwise give rise to other symptoms and an acute phase of illness, known as the dual-vulnerability hypothesis, is beginning to receive some support in the seasonal affective disorder literature (Young, Reardom & Azam, 2008). The current study appears to be the first to provide evidence for this type of process in a prospective, longitudinal study of unipolar depression. Future studies, hypothesizing specific vulnerabilities and testing patterns of symptom onset, are needed to continue to support this theory.

The notion that the prodromal symptoms of depression could represent the core syndrome of the episode also has applicability in identifying subtypes of depression. Toward this end, the current study supported the hypothesized hopelessness subtype of depression, as well as the process by which one develops a hopelessness depression. Among episodes that qualified for hopelessness depressions, the symptom of hopelessness reliably appeared earliest, followed by sad mood, self-blame, brooding/worry, decreased self-esteem and dependency. These are also

generally the latest symptoms to remit, with hopelessness and decreased self-esteem typically remitting near the very end. This supports the role of hopelessness in these episodes as well as the hopelessness subtype of depression in general. This also supports the notion of dual vulnerabilities. Here, hopelessness is triggered earliest, which in turn triggers vulnerability for other, specific symptoms. As the episode remits, secondary symptoms remit first, followed by the core symptoms, with hopelessness and decreased self-esteem remitting latest in the process.

Interestingly, results from episodes that met criteria for endogenous depression support the general model- that a core syndrome presents earliest and remits latest- but did not support the hypothesis that the core syndrome would be specifically related to the nature of the subtype. This might be explained by the dual-vulnerability theory. In this framework, initial vulnerability triggers symptoms of hopelessness, decreased self-esteem, sad mood, decreased interest or pleasure and decreased initiation of voluntary responses- these symptoms also remained as the latest to remit. The vegetative symptoms associated with endogenous depressions, and based on which diagnoses were made among these episodes, appeared during the acute phase of the episode as secondary symptoms. Individuals with endogenous depression episodes might have had specific vulnerabilities that, when triggered, led to the emergence of a specific constellation of symptoms. These, in turn, triggered another vulnerability for the vegetative and other symptoms specific to the endogenous subtype. These secondary symptoms were among the first to remit, with the primary symptoms remitting later. Unfortunately, the methods available in the current study cannot provide specific evidence for such a complicated process. However, the results are suggestive and should be replicated and followed with research into the possibility of dual vulnerabilities acting during a depressive episode.

A negative cognitive style, sociotropy, and autonomy were also examined for their role in the development of specific prodromal and residual symptoms of depression. Analyses of the role of a negative cognitive style supported the hypothesis that the earliest and latest symptoms

present would be specifically related to the underlying process- here a negative cognitive style, which is hypothesized to predispose an individual to specific (hopelessness) depressive symptoms- but did not demonstrate a consistency between the symptoms earliest to present and latest to remit. Conversely, autonomy was observed to predict a unique set of symptoms that remained consistent between the prodromal and remission phases, but these symptoms were not among those empirically associated with this cognitive-personality characteristic. This could be due to the heterogeneity of the factors comprised by the measure of autonomy used in this study. Sociotropy did predict a constellation of symptoms, decreased interest or pleasure, crying more and self-pity, that were the earliest to present and latest to remit among high- versus low-sociotropy individuals. This suggests that the "core sense of deprivation" of the depressed sociotropic individual appears early in the depressive episode and remains throughout, and these symptoms are among the latest to remit, highlighting the role of this syndrome as the core of the depressive experience for these individuals.

Taken together, results from this study support the existence and role of the depressive prodrome. In this phase of the episode, the earliest symptoms to appear are thought to form the core of the depression, are generally consistent throughout the episode, and remain as the last to remit. Indeed, the order of symptom onset appears to be related to the reverse of the order of symptom remission. Moreover, the durations for the prodromal and remission phases are significantly correlated. Thus, the general model tested has been supported by these results. When applied to the hopelessness subtype of depression, and depressions experienced by highly sociotropic individuals, the model holds. In the endogenous subtype of depression, and among cognitively high-risk and highly autonomous individuals, the model was not strongly supported. Future research is warranted to further examine the role of prodromal symptoms in the course of a depressive episode, to examine the role of cognitive and personality predictors of specific prodromal symptoms, and studying preventive treatments for depression aimed at prodromal

symptoms as well as treatments for an acute episode that target the core syndrome as identified by prodromal symptoms.

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