The Characteristics of Depressive Subtypes Among Adolescents and Their Role in the Relationship Between Weight and Depression

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Dissertation submitted in fulfillment of the requirements for the degree of Doctorate of Philosophy in the Department of Psychology in the Graduate School of Duke University

2009
ABSTRACT

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Abstract

For several decades, researchers have sought to fully understand the nature of the relationship between depression and weight. To date, the research in this area has yielded highly inconsistent results, with some identifying null (Crumpton, Wine, & Groot, 1966; Moore, Stunkard, & Srole, 1962), positive (R. E. Roberts, Kaplan, Shema, & Strawbridge, 2000), negative (Silverstone, 1968; Simon, 1963) and gender specific relationships (DiPietro, Anda, Williamson, & Stunkard, 1992; Istvan, Savela, & Weidner, 1992; Onyike, Crum, Lee, Lyketsos, & Eaton, 2003). The author suggests that these inconsistencies can be explained by the use of measures of depression that do not differentiate between various subtypes of depression which are associated with divergent somatic symptoms; including atypical depression (AD) and melancholic depression (MD). Adolescence may be an important intervention point to avert adult obesity and identification of subtypes may identify those at greatest risk. Yet, the characteristics of depression subtypes among adolescents are unknown. In order to identify subtypes of depression among adolescents that are differentially associated with weight, Latent Class Analysis (LCA) was conducted and resulting classes were tested for associations with weight. Six latent classes were identified. Four were uniquely associated with somatic symptoms including hyper- and hypophagia, suggesting that somatic symptoms play an important role in the distinction between depressive
subtypes. Analyses showed an association with BMI for the 2 hyperphagic classes but not for the 2 hypophagic classes. The inclusion of depression class improved the fit of regression models for depression predicting BMI. This suggests that the inclusion of depression subtype in analyses may clarify the association between weight and depression.
Dedication

This work is dedicated to my parents who nurtured my interest in science and psychology and supported me through it all.
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1. Introduction

Obesity and depression are the most common chronic medical and psychological illnesses in the United States (WHO, 2004). Children and adolescents are the fastest growing demographic for both conditions (The Cross National Collaborative Group, 1992). Both disorders are important public health concerns due to the significant physical (Kessler, Zhao, Blazer, & Swartz, 1997; Must et al., 1999) and psychological impact (Wardle & Cooke, 2005) on affected individuals, as well as the economic impact in the employment (Burton, Chen, Schultz, & Edington, 1998; Conti & Burton, 1994; W. F. Stewart, Ricci, Chee, Hahn, & Morganstein, 2003) and health care sectors (Colditz, 1992; Greenberg et al., 2003; Wang & Dietz, 2002). Recent trends in obesity are similar to those observed in depression: both have increased sharply during the past 50 years (Fombonne, 1994; Klerman & and Weissman, 1989; The Cross National Collaborative Group, 1992; Flegal, Ogden, Carroll, & Johnson, 2002; Flegal, Kuczmariski, Johnson, 1998; Kuczmariski, Campbell, Johnson, 1994; Mokdad et al., 1999), the prevalence of both is rapidly increasing in adolescent populations (Blazer, Kessler, McGonagle, Swartz, 1994; Hedley et al., 2004; Ogden, Flegal, Carroll, & Johnson, 2002b), and both are most prevalent among women (Flegal et al., 2002; Kessler, McGonagle, Swartz, Blazer, & Nelson, 1993; Kessler, 2003; Narrow, Rae, & Regier, 1998; Ogden et al., 2002b) as well as individuals of lower socioeconomic status (Berkham & Breslow, 1983; Bruce, Takeuchi, & Leaf, 1991; Gortmaker, Must, Perrin, Sobol, & Dietz, 1993; Kaplan, Roberts, Camacho, & Coyne, 1987; Lynch, Kaplan, & Salonen, 1997; Roberts, Stevenson, and Breslow, 1981;
Sobel & Stunkard, 1989; Stansfeld & Marmot, 1992). These similarities lend support to the hypothesis that weight, particularly excess weight, and depression may be related (Faith, Matz, & Jorge, 2002); however, thus far a consensus on the nature of this relationship has not been reached as research findings have been surprisingly inconsistent. Greater understanding of the clustering of the somatic symptoms of depression, which are most likely to contribute to changes in weight, may clarify this relationship. Should one or more classes associated with particular somatic symptoms (appetite, sleep, activity level) be identified and a consistent relationship with weight change established; it would inform obesity and depression prevention, aid in treatment selection, and possibly improve treatment outcomes for both disorders.

1.1 Issues in Obesity

Although the prevalence of obesity is increasing across age, socioeconomic, and ethnic groups, recent increases among children and adolescents are a particular public health concern. Since the 1970s, the prevalence of overweight has doubled among children aged 2 to 5 years and tripled among children aged 6 to 19 years. Results from the 1999-2002 National Health and Nutrition Examination Survey (NHANES) indicate that nearly 16% of youths between the ages of 6 to 19 years are overweight; nearly double the prevalence from estimates just one decade before (Hedley et al., 2004; Ogden, Flegal, Carroll, & Johnson, 2002a).
Obesity has a significant negative impact on both the physical and emotional health of youth. The recent increases in the prevalence of type 2 diabetes in children and adolescents can be almost entirely attributed to increased obesity in that population (Dabelea, Pettitt, Jones, & Arslanian, 1999; Pinhas-Hamiel, Dolan, & Daniels, 1996; Rosenbloom, Joe, Young, & Winter, 1999). Obesity in childhood and adolescence is associated with increased risk for multiple health conditions (Balcer et al., 1999; Dietz, Gross, & Kirkpatrick, 1982; Lauer, Connor, & Leaverton, 1975; Marcus et al., 1998; Palasciano et al., 1989; Sorof & Daniels, 2002; Unger, Kreeger, & Christoffel, 1990). The health outcomes of obesity only worsen among adults, with a two-fold increase in mortality, as well as serious cardiac, endocrine, rheumatologic and vascular neurologic comorbidities (Must, Jacques, Dallal, Bajema, & Dietz, 1992). Obesity is also associated with poor psychosocial outcomes. The social stigma associated with obesity can result in chronic guilt, shame and embarrassment (Friedman & Brownell, 1995) as well as a consequent increased risk for low self-esteem (Sheslow, Hassink, Wallace, & DeLancey, 1993). Obese children experience more teasing, aggression (Gortmaker et al., 1993; Neumark-Sztainer et al., 2002; Strauss & Pollack, 2003) and isolation (Neumark-Sztainer, Story, & Faibisch, 1998) compared to their normal weight peers. Not only are these consequences independently associated with poor health outcomes and quality of life, but several, including low self-esteem and social isolation, have also been independently linked to depression.
1.2 Issues in Depression

While not as prevalent as obesity, Major Depressive Disorder (MDD) is the most prevalent psychological disorder in the United States. The one-year prevalence of MDD among adults is estimated at 5.3% (Blazer, McGonagle, & Swartz, 1994; Kessler et al., 1997; Riolo, Nguyen, Greden, & King, 2005). One-year prevalence of major depression in adolescents may be even higher; in some studies as high as 8.3% (Anderson & McGee, 1994; Garrison et al., 1997; Kessler & Walters, 1998; Lewinsohn et al., 1994). Like obesity, depression has shown notable increases in prevalence during recent decades accompanied by demographic changes in prevalence that closely mirror those of obesity (Flegal, Carroll, Kuczmarski, & Johnson, 1998; Flegal et al., 2002; Fombonne, 1994; Klerman & Weissman, 1989; R. J. Kuczmarski, Flegal, Campbell, & Johnson, 1994; Mokdad et al., 1999; The Cross National Collaborative Group, 1992). Trends in major depression show increasing incidence and earlier onset than ever before (Joyce, Oakley-Browne, Wells, & Bushnell, 1990), as well as dramatically increased rates of depression during adolescence (Roza, Hofstra, van der Ende, & Verhulst, 2003). Epidemiological data suggest that the prevalence of depression among children and adolescents has more than doubled across age groups during the past 30 years (Blazer et al., 1994).

The consequences of depression among children and adolescents are significant and potentially sustained into adulthood. Adolescents with depression have greater risk for impulsive risk taking behavior (DiClemente et al., 2005; Glied & Pine, 2002). During the episode of depression, children and adolescents with MDD frequently experience
impairment in school performance (Birmaher et al., 1996) and relationships with others (Asarnow & Ben-Meir, 1988; Asarnow, Carlson, & Guthrie, 1987; Kashani, Burbach, & Rosenberg, 1988; Puig-Antich et al., 1993; Puig-Antich et al., 1985; Rao et al., 1995; Strober, Lampert, Schmidt, & Morrell, 1993). Moreover, adolescents with two or more depressive episodes appear to have poorer long-term functioning, while adolescents with non-recurrent MDD, if treated, may have good psychosocial outcomes similar to normal controls (Rao et al., 1995).

Given the negative physical and psychosocial impact of obesity and depression and their possible association, a considerable amount of research has been conducted on the relationship between weight and depression. However, despite the depth and breadth of research on the subject, no clear conclusions about the relationship between the two can be made, as the research to date has shown inconsistent results (Faith et al., 2002; Friedman & Brownell, 1995; A. Stunkard & Wadden, 1992). This research has used several different measures that operationalized depression in a range of ways. Some assessments included bi-directional somatic symptoms, some only assessed for loss of appetite, insomnia and psychomotor agitation and some did not assess somatic symptoms at all. In addition to diverse results, a handful of studies found a significant positive association between weight and depression in women, but not in men (Istvan et al, 1992, DiPietro et al, 1992, Carpenter et al., 2000, Onyike et al., 2003), and one study indicated that the relationship between weight and depression only exists for those in the highest ranges of BMI (Dong, Sanchez & Price, 2004), painting an increasingly
complex relationship between weight and depression. Various researchers have attempted to explain these contradictory results by citing differences in sample populations (Onyike et al., 2003), varied measures of weight status and depression (Friedman & Brownell, 1995), gender differences (Carpenter, Hasin, Allison, & Faith, 2000; Istvan et al., 1992; Noppa & Hallstrom, 1981), age differences (Adams et al., 2006) and socioeconomic differences (Ross, 1994; Stunkard, Faith, & Allison, 2003). However, results remain inconsistent even when examining research within similar populations and using similar measures (DiPietro et al., 1992; Istvan et al., 1992).

One possible explanation of such inconsistent associations between depression and weight that has not yet been considered is that these inconsistencies may be due to the heterogeneity of the current definition of depression. Currently depression is defined by both mood and somatic symptoms. Mood symptoms in the diagnosis of depression are unidirectional. In fact, when bi-directional mood symptoms are present, the patient is given a different label: bipolar disorder. However, currently the somatic criteria for depression allow for three bi-directional symptoms: changes in appetite, sleep patterns and activity levels. Although an association between depression and weight that is mediated by mood symptoms is possible, somatic symptoms are the most likely mediators between any association of weight and depression, particularly as all three play a role in metabolic energy balance. However, given that the direction of change in somatic symptoms of depression alters the energy equation into either a positive (weight gain) or negative (weight loss) state, it is equally likely that an individual who
meets current diagnostic criteria for depression will lose or gain weight dependent on
the direction of any somatic symptoms. This is not to say that depression is not
associated with weight. Rather the nature of our current diagnostic criteria for
depression makes weight change likely in this population, but does not allow for the
prediction of the direction of weight change. By utilizing a definition of depression that
affords equal weight to any change in physiologic symptoms regardless of direction,
researchers have likely been nullifying their results when examining this relationship.
2. Depressive Subtypes as Unique Syndromes

2.1 The Characteristics of Depression Subtypes

There is considerable evidence that depression may represent both a dimensional and a taxometric structure, with a few distinct phenotypic presentations that are also dimensional in nature. While not independent diagnoses, the most recent version of the diagnostic and statistical manual, DSM-IV-TR (American Psychiatric Association, 2000) provides “atypical” and “melancholic” specifiers as supplementary descriptors to a diagnosis of MDD. The symptom profiles of these two subtypes contain unidirectional somatic symptoms likely to contribute to weight gain or weight loss. Full diagnostic criteria for melancholic depression (MD) includes: severe and unreactive anhedonia, distinct quality of depressed mood, depression regularly worse in the morning, early morning awakening, marked psychomotor retardation or agitation, significant anorexia or weight loss and excessive or inappropriate guilt. The criteria for atypical depression (AD) are largely antithetical to those of MD: mood reactivity, weight gain, hyperphagia, hypersomnia, leaden paralysis (i.e. heavy feelings in the arms or legs), and interpersonal sensitivity. There exists some question as to the validity of the currently accepted diagnostic characteristics. However, research tends to support the phenotype model and unique groups characterized by somatic symptoms consistent with melancholic and atypical features have been repeatedly identified (Ambrosini, Bennett, Cleland, & Haslam, 2002; Beach & Amir, 2003; Benazzi, 2000; Grove et al., 1987; Haslam & Beck, 1994; M. Thase, Hersen, Bellack, & Himmelhock, 1983).
Greater controversy exists concerning whether depressive subtypes are valid clinical entities among children and adolescents. For many years, experts hypothesized that melancholic depression occurred so rarely among children and adolescents that it did not merit study (Parker & Roy, 2001; Patton, Coffey, Posterino, Carlin, & Wolfe, 2000; Rao et al., 1995). However, several taxometric studies showed evidence of a melancholic subtype among children and adolescents (Kolvin et al., 1991; Ryan et al., 1987). Greater consensus exists on the relevance of the AD subtype among youth, however research has failed to validate the diagnostic criteria in this population (Williamson et al., 2000). As these subtypes have not been validated among adolescents it is necessary to establish symptom classes that, though informed by previous research with adults, have not had adult profiles imposed upon them. Only then can the association between adolescent depression classes and weight be examined in order to accurately identify those patients most at risk for weight change.

2.2 Atypical Depression as a Distinct Diagnostic Entity

While currently the term atypical is used specifically to describe a group of symptoms that are less common among depressed individuals; more recent research suggests that AD and Non-AD (which includes MD) may be related, yet distinct disorders, much in the way that type 1 and type 2 diabetes mellitus are similar in their presentation (polyuria, polydypsia etc) but different etiologically and require somewhat differential treatment. AD is differentially associated with several psychosocial
characteristics including female gender (Matza, Revichi, Davidson, & Stewart, 2003; J. W. Stewart, McGrath, Rabkin, & Quitkin, 1993), more recurrent episodes (Nierenberg, Alpert, Pava, Rosenbaum, & Fava, 1998), and younger age (Quitkin, McGrath, Stewart, & Klein, 2003; J. W. Stewart, McGrath, & Quitkin, 2002). Several studies have also demonstrated consistency across episodes for AD and Non-AD groups (Kendler et al., 1996; Stunkard, Fernstrom, Price, Frank, & Kupfer, 1990; Sullivan, Kessler, & Kendler, 1998). Overall, these differential characteristics support the hypothesis that AD is categorically unique from other types of depression.

In addition to unique psychosocial correlates, the results of several studies suggest that AD is a biologically unique type of depression. Research has shown that individuals with an AD symptom profile require more time to fall asleep, are four times more likely to report chronic pain symptoms, including headache and stomach ache and are three times more likely to report significant fatigue (Silverstein, Cohen, & Kasen, 2006). Several studies have cited increased effectiveness for treatment with MAOIs (Larsen et al., 1991; Lonnqvist, Sihvo, Syvalahu, & Kivururu, 1994; McGrath et al., 1992; Quitkin et al., 1993; Robins & Guze, 1970; Sogaard et al., 1999) and cognitive behavioral treatments (CBT) (Jarrett et al., 1999), as well as select selective serotonin reuptake inhibitors (SSRIs) (McGrath et al., 1992), compared to tricyclic medications in individuals exhibiting AD symptoms. In addition, neurologic differences between AD and Non-AD subjects have been well documented (Levitan, Vaccarino, Brown, & Kennedy, 2002;
2.2.1 Examination of the Atypical Depression Symptom Cluster

Several studies using cluster analysis have identified a depression class associated with increased appetite and weight gain, most often labeled atypical depression. Latent class analysis of a twin sample revealed three clinically significant depressive syndromes: mild typical depression, atypical depression, and severe typical depression. In a study using data from the National Twin Registry, the severe typical depression class was characterized by comorbid anxiety and panic, longer episodes, greater impairment, and help seeking. In contrast, that atypical depression class was characterized by fewer comorbidities, hyperphagia, hypersomnia, frequent and relatively short episodes, and obesity (Sullivan et al., 1998). Latent class analysis of data from the National Comorbidity Study revealed six classes of depression that were either categorically or dimensionally unique. Two of these classes were identified as atypical. These classes were associated with both insomnia and hypersomnia, personality traits of increased dependency and lower self-esteem. Two additional classes were associated with MD type symptoms such as weight loss, insomnia, anergia and poor concentration.
Although the authors identified these two classes as “typical” depression, vegetative symptoms distinguished these two classes.

Sullivan and colleagues (1998) noted that the differential characteristics identified for AD compared to Non-AD samples resembled a functional shift of somatic symptoms; with AD characterized by increases in weight, appetite, sleep and psychomotor retardation and Non-AD characterized by the opposite: decreased weight, appetite and sleep, as well as increased psychomotor agitation. More importantly, mood reactivity and interpersonal sensitivity were not uniquely associated with AD. Based on their research, Sullivan and colleagues concluded that AD is a valid clinical entity independent of Non-AD that is characterized by hyperphagia, hypersomnia, psychomotor retardation, as well as extended duration and chronicity.

Benazzi examined depressive symptoms using the SCID (First, Spitzer, & Gibbon, 1997) and Global Assessment of Functioning (GAF). After mood reactivity (which was a diagnostic requirement), leaden paralysis and interpersonal rejection sensitivity were the most common symptoms in the AD sample, though all atypical symptoms were significantly associated with an AD diagnosis (Benazzi, 2003). In a 2005 follow-up, Benazzi attempted to identify key differentiating features of AD using factor analysis. Three factors were identified. The first included reversed vegetative symptoms (oversleeping, overeating and weight gain, and leaden paralysis) and was negatively correlated with weight loss and decreased eating. The second included interpersonal
sensitivity, leaden paralysis, fatigue and diminished ability to concentrate. Finally, the third included mood reactivity and was negatively associated with thoughts of death and worthlessness. All criteria for AD except mood reactivity significantly predicted membership in the AD class. The authors found that the first factor, characterized by reverse vegetative symptoms, was the only factor significantly associated with identified validators of AD (such as female gender, early age of onset, and family history). They suggested that these reverse vegetative symptoms may have more diagnostic validity than the current DSM-IV requirement of mood reactivity, which was not more strongly associated with AD compared to Non-AD (Benazzi, 2005).

In 2002, Posternak and Zimmerman examined the characteristics of AD in 479 psychiatric outpatients diagnosed with MDD (Posternak & Zimmerman, 2002). In this sample, AD was associated with younger age at onset, female gender, longer episode duration and greater severity of illness. In addition, patients with AD were more likely to experience psychomotor retardation and reversed diurnal variation, compared to individuals with Non-AD. Also of note, although mood reactivity was the most common symptom in the AD sample, it was not associated with a greater likelihood of meeting the AD diagnostic threshold; whereas, “reverse vegetative symptoms” (hyperphagia, hypersomnia and leaden paralysis) were significantly associated with atypical diagnosis. This finding suggests that while most individuals who experience atypical depression also experience mood reactivity, this symptom is not unique to individuals with an AD
presentation, whereas the reverse vegetative symptoms are unique to an atypical presentation.

Finally, in 2003, Matza, Revicki, Davidson and Stewart found that individuals with AD reported higher rates of hypersomnia and increased appetite compared to those with Non-AD. The AD group also reported significantly higher rates of most depressive symptoms, feelings of worthlessness, anhedonia, suicidal thoughts and attempts, psychiatric co-morbidities, disability and restricted-activity days, and use of health care services. In addition, the AD group had significantly higher rates of parental depression, and childhood neglect or abuse compared with the Non-AD group and a group that had no history of psychiatric disorders. Those identified as Non-AD reported insomnia and hypophagia at a rate much higher than any other symptom of depression, suggesting that AD and Non-AD may be best differentiated by their somatic symptoms. In order to test the validity of their somatic symptom differentiation hypothesis, Matza and associates identified patients with AD based only on the somatic symptoms of hypersomnia and hyperphagia. They compared this AD group with a group who had Non-AD and with a group who had no psychiatric disorder. Results indicated that somatic symptoms alone are effective at identifying patients with AD and may be better markers for AD than the full DSM-IV criteria (Matza et al., 2003).

The research to date clearly identifies a unique symptom profile for depression characterized by reverse vegetative symptoms (hypersomnia, hyperphagia and leaden
paralysis)(Thase, Carpenter, Kupfer, & Frank, 1991), in addition to the non-distinguishing symptoms of mood reactivity and interpersonal sensitivity. The central role of hyperphagia and hypersomnia in characterizing AD suggests that weight gain is a likely outcome of AD episodes, particularly given the chronic and recurrent nature of AD. Taken together, this research suggests that the AD diagnosis is a valid and distinct depression profile, uniquely characterized by decreased activity levels, hypersomnia, and hyperphagia; characteristics likely to be associated with weight gain.

2.2.2 Atypical Depression in Adolescence

Research has consistently shown that AD is characterized by an early age of symptom onset. In fact, onset of depressive symptoms in teenagers or patients in their early 20s is more likely to be characterized by AD symptoms rather than Non-AD symptoms (Stewart et al., 2002; Stewart, Quitkin, McGrath, & Klien, 2005; Thase, 1997). This, combined with findings from the adult literature that AD is best characterized by reversed vegetative symptoms, is more likely to be chronic than Non-AD (Quitkin et al., 2003) and that type of depression tends to be consistent across episodes (Kendler et al., 1996; A. J. Stunkard et al., 1990; Patrick F. Sullivan, Prescott, & Kendler, 2002), suggests that individuals who are vulnerable to AD are at risk for obesity from a fairly early age. Weight would be likely to increase with each depressive episode, accumulating over the lifetime of the individual with AD.
The implications of an early onset of AD suggest that adolescence may be a key intervention point both to limit the chronicity of the disorder, as well as subsequent chronic obesity resulting from the somatic symptoms of AD. However, though several studies have begun to establish an empirically validated definition of AD in adults, only one study has examined the characteristics of AD in adolescence. Williamson and colleagues examined the presence of AD symptoms in a sample of 1046 youths aged 6 to 19 years who all met criteria for MDD using the K-SADS. While 15.5% of the sample met criteria for AD, DSM-IV AD symptoms were found to correlate only marginally suggesting that the adult definition of AD has only marginal construct validity among children and adolescents (Williamson et al., 2000). Thus, though initial onset of AD is typically during adolescence and therefore adolescence represents a potentially important intervention point, it appears that the use of adult characteristics to identify adolescent AD is not optimal. Therefore, identifying the characteristics of AD in adolescents becomes an imperative both for the treatment of depression in this population, as well as for the prevention of depression-related obesity.

2.3 Melancholic Depression as a Distinct Diagnostic Entity

The melancholic subtype of depression is also likely to be associated with changes in weight. In contrast to AD, examination of the symptom profile of MD indicates a significant role for severe anhedonia, psychomotor abnormalities, decreased appetite, and terminal insomnia (Benazzi, 2002b; Kendler, 1997; Khan et al., 2006;
Melartin, Leskela, Petteri, Lestela-Mielonen, & Isometsa, 2004; Rush & Weissenburger, 1994; Spallone et al., 1999). Studies utilizing taxometric analyses in adults have isolated specific clinical features that define a melancholic class of depression that is qualitatively distinct from non-melancholic symptomatology (Ambrosini et al., 2002; Beach & Amir, 2003; Grove et al., 1987; Haslam & Beck, 1994). In three studies, a presentation consistent with MD was observed in approximately 40% of the sample. In a sample of more than 250 depressed inpatients and outpatients, melancholic depression was most clearly distinguished from the residual nonmelancholic class by the presence of motoric disturbance (Parker et al., 1999; Spallone et al., 1999).

The MD profile is differentially associated with particular symptomatic and demographic characteristics and comorbidities. Generally, patients fitting the MD class tend to be older (M. E. Thase & Friedman, 1999; Van Praag & Plutchik, 1984). In fact, elevated rates of MD with age have led some to propose that biological correlates of aging may play a role in producing melancholic symptoms (Benazzi, 2002a). Episodes are characterized by shorter duration, elevated severity (Khan et al., 2006), fewer co-morbid axis II diagnoses (Shea, Glass, Pilikonis, Watkins, & Docherty, 1987; Tedlow et al., 2002), and lower levels of neuroticism (Kendler, 1997). MD is associated with a nearly even gender distribution, fewer bipolar diagnoses and increased overall symptom endorsement (Benazzi, 2002a). Adults with MD, compared to depressed adults without MD, have a worse prognosis, an increased duration of depression (Grove et al., 1987), increased noradrenergic output (Roy, Pickar, Linnoila, & Potter, 1985), a tendency
to exhibit nonsuppression of cortisol during the dexamethasone suppression test (Rush & Weissenburger, 1994), worse psychosocial functioning (Lafer, Nierenberg, Rosenbaum, & Fava, 1996), and better response to antidepressant treatment in several, though not all, studies (Free & Oei, 1989; Klerman, Weissman, & Prusoff, 1982; Rush & Weissenburger, 1994). Interestingly, individuals with MD are less likely to respond to placebo than non-melancholic patients (Peselow, Sanfilipo, & Difiglia, 1992) which may be an artifact of the intractable anhedonia noted in this population.

### 2.3.1 Melancholic Depression in Adolescents

There is a longstanding debate regarding whether melancholic depression occurs with enough frequency among children and adolescents to merit study (Parker & Roy, 2001; Patton et al., 2000; Rao et al., 1995). However, although this subtype may be less prevalent among adolescent populations when compared to adults, studies of adolescents have revealed notable evidence of the presence of a melancholic subtype among children and adolescents (Ambrosini et al., 2002; Kolvin et al., 1991; Ryan et al., 1987) with prevalence ranging between 20 and nearly 50%. Carmanico and colleagues identified a predominantly MD cluster of depressive symptoms, characterized by high ratings of dysphoric mood, decreased interest, weight and sleep disturbance, fatigue, guilt, suicidal ideation, and negative attributions. This group also endorsed the highest frequency of symptoms on all subscales (75%-96%)(Carmanico et al., 1998). Interestingly, Ryan and colleagues identified a melancholic factor among adolescents but not among prepubertal depressed children (Ryan et al., 1987). In contrast, Ludy and colleagues
(2004) found evidence for a melancholic subtype among preschool children, suggesting that a cluster of MD symptoms can be found across age groups.

Adolescents with MD have shown equal gender distribution (Carmanico et al., 1998), increased comorbid anxiety symptoms (Wood, Harrington, & Moore, 1996) and may have a shorter REM latency following the onset of sleep (Emslie, Rusha, Weinberg, Rintelmann, & Roffwarg, 1994) compared to other depressed adolescents. These findings are consistent with both the sleep disturbance and motoric changes associated with MD. Adolescents diagnosed with MD show poor response to psychosocial treatment without pharmacotherapy (Robbins, Alessi, & Colfer, 1989). These results suggest not only that MD does occur in adolescents, but that its unique profile and associated characteristics supports its utility as a diagnostic entity in this population.
3. Previous Examination of the Association between Weight and Unipolar depression

3.2 The Research to Date

3.2.1 Early Research

Early research examining the relationship between weight and depression hypothesized that the relationship between weight and unipolar depression would express itself as less depression in the obese and that obese individuals would alleviate intrapsychic conflicts via food consumption. Thus, researchers expected the obese to exhibit less depression because they had an effective way to alleviate their distress.

Research founded on this assumption was fairly consistent: it either revealed no relationship between weight and depression (Crumpton et al., 1966; Moore et al., 1962) or it revealed a negative association, which researchers suggested meant that obesity might be a protective characteristic for depression (Silverstone & Lascelles, 1966; Simon, 1963).

There are several methodological flaws present in these studies that make interpretation of the results difficult. First, all but one of these studies (Moore et al., 1962) failed to examine the relationship between obesity and mental health in a representative sample. Study samples were taken from students in a rural school (Burchinal & Eppright, 1959), clinic attendees (Fink, Gottesfeld, & Glickman, 1962; Leckie & Withers, 1987; Silverstone & Lascelles, 1966) and military personnel (Simon, 1963), which strongly
limits the generalizability of these findings. Many of these samples did not include both genders and nearly all were ethnically homogeneous.

In addition, the methods of classifying weight status in many of these studies are not comparable to classifications currently used. In fact, in every study that described their criteria for obesity in detail, many of those who were identified as obese would not be classified as such by today’s standards based on the Body Mass Index (BMI) (National Institutes of Heath, 1998). In fact, one study identified participants who would have a normal weight by today’s standards (BMI between 18 and 25), as obese (Silverstone & Lascelles, 1966). Several of these studies did not include participants in the upper ranges of BMI (>40) and may not have collected a wide enough range of weights to reveal a significant effect. Several studies to be discussed later in this review have revealed that risk for depression is especially high for those in the highest ranges of BMI. Therefore, a sample with a range of BMI, including severely obese individuals, is important for a complete understanding of any relationship between weight and depression.

Finally, and perhaps most importantly, these studies lacked valid and specific measures of depression. As the original DSM did not include an inventory of symptoms indicative of the disorder, nor clearly differentiate depression from anxiety, no agreed upon symptoms for depression were available. Thus, researchers identified depression in a myriad of ways including unspecified interview (Fink et al., 1962; Moore et al., 1962) and author determined lists of symptoms for depression (Simon, 1963). Some included
assessment of symptoms not exclusive to depression (Burchinal & Eppright, 1959; Silverstone & Lascelles, 1966), most did not include assessment of the somatic symptoms of depression in their measures and many did not include any behavioral symptoms of depression. Instead, nearly all of the measures of depression in these studies focused on the emotional symptoms of depression and some of the cognitive distortions commonly associated with depression. When the currently accepted somatic symptoms of depression were considered in the identification of depression, the assessment of these symptoms was often incomplete. For example, Simon (1963) included hypophagia and insomnia as criteria for depression, but did not assess participants for hyperphagia and hypersomnia; symptoms likely to cause weight gain. This likely biased the results toward identification of a negative relationship between depression and weight.

Overall, the constructs being examined, both depression and weight status were different than those commonly used today and often biased the results toward confirmation of the author’s hypotheses. Even the few studies conducted during this period that yielded positive results (Fink et al., 1962; Leckie & Withers, 1987) were characterized by poor methodological design. Therefore, though such research may contribute to our understanding of the relationship between depression and obesity, the results are not definitive and are extremely difficult to interpret.

3.2.2 The Second Wave

Later research in this area became more experimentally and methodologically
rigorous as validated measures of depression were used and potential covariates were controlled for. Experimental designs expanded to longitudinal and population-based, in addition to cross-sectional clinical studies. However, the research used several different measures of depression that operationalized depression in a range of ways. Not surprisingly, this yielded more diverse results, as some assessments included bi-directional somatic symptoms, some only assessed for loss of appetite, insomnia and psychomotor changes and some did not assess somatic symptoms at all. In addition to generally diverse results, a handful of studies found a significant positive association between weight and depression in women, but not in men (Carpenter et al., 2000; DiPietro et al., 1992; Istvan et al., 1992; Onyike et al., 2003), and several more indicated that the relationship between weight and depression only exists for those in the highest ranges of BMI (Dong, Sanchez, & Price, 2004), painting an increasingly complex relationship between weight and depression.

3.2.2.1 The Role of Type of Symptom Assessment

One of the most salient limitations of the research on weight and depression to date is the inconsistency with which symptoms were assessed. Differences in findings are potentially attributable to the measure selected to assess depression. For example, The Center for Epidemiologic Studies Depression scale (CES-D)(Radloff, 1977), which does not assess any reverse vegetative symptoms, showed no or only small associations between depression and weight (DiPietro et al., 1992; Istvan et al., 1992; Ross, 1994).
Similarly, the original Beck Depression Inventory (BDI);(Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) assesses only vegetative symptoms of depression. Thus, individuals who experience reverse vegetative symptoms of depression will have lower BDI scores compared to similarly severe individuals with decreased appetite and sleep. Therefore, it is not unexpected that Faubel found no association between obesity and depression(Faubel, 1989) and that Palinkas and colleagues found a negative association between weight and depression as assessed by the original BDI (Palinkas &Wingard, 1996). However, Fabricatore and colleagues found a weak positive association between BDI-II (Beck, Steer, Ball, & Ranieri, 1996) scores and BMI (Fabricatore, Wadden, & Sarwer, 2003). In contrast to its predecessor, the BDI-II contains items that assess for both vegetative and reverse vegetative symptoms, although it does not account for these differences in scoring.

The duration of symptoms assessed by each measure must also be considered when selecting a measure for research on weight and depression. The CES-D only assesses for symptoms occurring within the past week, further contributing to its unsuitability for research in this area. A similar assessment of brief duration symptoms, the DSM 12D may be similarly problematic. Roberts and colleagues (R. Roberts, Strawbridge, Deleger, & Kaplan, 2002) used the DSM 12D in their longitudinal epidemiologic study. The DSM 12D only assesses depressive symptoms over the previous 2 weeks. This may in part explain why results indicated no cross-sectional relationship but did reveal a longitudinal relationship wherein obesity predicted future
depression. The DSM 12D, like the CES-D risks elevated rates of transient depression, which, even when somatic symptoms are present, would not lead to notable changes in weight in either direction.

Finally, the way in which weight status is assessed may also play a significant role. In a study of adults, BDI-II scores were found to be significantly associated with measures of obesity when waist to hip ratio (WHR) was used as an indicator of obesity instead of BMI (Ahlberg et al., 2002; Haukkala & Uutela, 2000) in both men and women, though the relationship was only maintained in women when BMI was used in place of WHR.

### 3.2.2.2 Controlling for Covariates

Several studies also provide evidence for the importance of covariates in understanding the association between weight and depression. Gender has shown to be particularly important in this area (Carpenter et al., 2000; DiPietro et al., 1992; Istvan et al., 1992; Onyike et al., 2003), even when less effective measures are used. Despite limitations in the CES-D’s specificity, two studies using the measure found a significant association between obesity and depression cross-sectionally in women, but not in men (DiPietro et al., 1992; Istvan et al., 1992). Although the CES-D does not assess for symptoms likely to contribute to weight gain, the higher level of prevalence of these symptoms among women (Posternak & Zimmerman, 2001) may have resulted in an effect strong enough among women to overcome this methodological gap.
BMI classification and age have also been shown as useful covariates. Dong and colleagues (2004) only found a positive association between weight and depression in the most severe ranges of obesity (Dong et al., 2004). Onyike and colleagues demonstrated a similar relationship with severity of obesity. When stratifying obesity into three separate classes, only the class with a BMI greater than 40 was associated with depression during the previous month. In contrast, when assessing the prevalence of obesity among treatment seeking women already diagnosed with MDD, the results indicated a higher prevalence of overweight but a lower prevalence of obesity when compared to population prevalence (Papakostas et al., 2004). Thus, in terms of prevalence, depression may be most prevalent at the highest levels of BMI and conversely only mild to moderate weight problems may be more prevalent in depressed samples.

3.2.2.3 The Contribution of Longitudinal Analyses.

Although data from cross-sectional studies has been weak (Faith et al., 2002; Friedman & Brownell, 1995; Hallstrom & Noppa, 1981; Needham & Crosnoe, 2005), longitudinal studies on the relationship between weight and depression have more consistently found an association between elevated BMI and depression; however, the direction of this association is not entirely clear. Several studies have demonstrated a prospective association between baseline obesity and depression at follow-up (Roberts et al., 2002; Roberts, Deleger, & Strawbridge, 2003; Roberts et al., 2000), while others have found that those who are depressed at baseline are at increased risk for obesity at
follow-up (Dallman, Pecoraro, & la Fleur, 2005; DiPietro et al., 1992; Goodman & Whitaker, 2002; Hasler, Lissek et al., 2005; Hasler, Pine et al., 2005; Oliver & Wardle, 1999; Stice, Presnell, Shaw, & Rohde, 2005; Wise, Adams-Campbell, Palmer, & Rosenberg, 2006). These findings indicate that relations between weight and depression may be bi-directional with depression contributing to weight change and obesity contributing to depression symptoms.

3.2.3 Research on Weight and Depression in Children

Research on the relationship between weight and depression among children is more sparse, though not surprisingly, the little research in this area has also shown inconsistent results. Initial research, using general mental health assessment measures, such as the Mental Health Analysis Test (Thorpe, Clarke, & Tiegs, 1946), examined the relationships of family relations and psychopathology with weight status, but no significant relationship was identified (Burchinal & Eppright, 1959; Tolstrup, 1953). As a result of the findings of these two studies, researchers concluded that obesity in children was the result of poor eating habits rather than any etiology of a psychological nature.

In contrast, more recent studies with follow-up data have demonstrated significant associations between obesity and depression. Although Pine and colleagues (Pine, Cohen, Brook, & Coplan, 1997) found no relationship between obesity and depression at baseline; a modest positive association among female participants and a negative association among male participants was identified at follow-up one year later. Goodman and Whitaker (Goodman & Whitaker, 2002) found that depressed mood was
associated cross-sectionally with BMI and classification of obesity at follow-up in a sample of 9000 participants. In addition, presence of depression at baseline more than doubled the risk of obesity one year later, even when the participants were not overweight or obese at baseline. The authors also examined the longitudinal relationship between obesity and subsequent depression, but these analyses were non-significant.

Several studies have examined the predictive relationship between weight and depression from adolescence to adulthood. The work of Mamun and colleagues suggests that the perception of being overweight during adolescence is a significant risk factor for depression in young adult men and women (Mamun et al., 2007). However, the majority of research in this area has demonstrated the reverse relationship (i.e. depression in adolescence as a potential risk factor for later obesity in adulthood) (Franko, Striegel-Moore, Thompson, Schreiber, & Daniels, 2005; Pine, Goldstein, Wolk, & Weissman, 2001; Richardson et al., 2003). Richardson and colleagues (2003) identified a relationship between the number of depression episodes during adolescence and risk for adult obesity. Pine and colleagues (Pine et al., 2001) found a small effect of adolescent depression on adult weight, but they also identified duration of childhood depression as a significant predictor of adult BMI, solidifying the validity of this modest effect. A study of female adolescents demonstrated a much stronger effect size as elevated depression symptoms were associated with a nearly four-fold increased risk of obesity at age 21 (Franko et al., 2005).
Similar to studies with adults, gender is a significant covariate in the relationship between weight and depression in adolescence. As mentioned above, Pine and colleagues (2001) identified an opposite relationship between weight and depression among girls and boys. Richardson and colleagues (2003) found that, while no association was found for male participants, depressed adolescent girls had a more than two fold increased risk for obesity in adulthood after controlling for initial BMI. Xie and colleagues (2005) found a significant association with elevated scores on the CES-D and higher BMI among female, but not male Chinese adolescents. Further analysis indicated that the relationship between depression and BMI in this sample was almost entirely mediated by perceived peer isolation. This suggests that the cross-sectional relationship between depression and weight may be dependent on psychosocial factors that are particularly salient for girls.

Overall, these data indicate that although it is unclear if adolescent obesity contributes to future depression (Goodman & Whitaker, 2002; Mamun et al., 2007), depressed adolescents consistently demonstrate an increased risk for the development and persistence of obesity into adulthood. The results of cross-sectional research examining the relationship between depression and obesity during adolescence are much more variable. Although, follow-up data from adolescents suggests that depression is associated with subsequent obesity, this relationship is much less robust in cross-sectional designs. However, it is important to note that most adolescents in these studies were in their first major depressive episode and therefore, any effect of
depression on weight may not have had time to accumulate, whereas at follow-up, enough time has passed to observe a relationship.
4. A Role for Depression Subtypes in the Relationship between Weight and Depression

All of the previously mentioned research examining the relationship between weight and depression fails to account for bi-directional somatic symptoms. This challenge in the examination of the relationship between weight and depression can be overcome by the inclusion of depressive subtypes, particularly MD and AD as covariates. Although no research testing an hypothesized relationship between depression and weight has been conducted using MD and AD as covariates, research empirically examining the characteristics of these two depression classes have frequently demonstrated lower weight among MD samples (Kendler, 1997; Khan et al., 2006) and have reliably demonstrated elevated weight among AD samples (Matza et al., 2003; McGinn et al., 1996; Posternak & Zimmerman, 2002). By not distinguishing between AD and MD, researchers may be nullifying significant results by combining groups likely to lose weight due to depressive symptoms with groups likely to gain weight due to the opposite symptoms.

The pattern of results in the literature supports this hypothesis. Measures of depression that assess for unipolar symptoms of MD but not AD somatic symptoms consistently indicate either a negative relationship or no relationship between weight and depression (Crisp & McGuiness, 1976; Crisp, Queenan, Sittampaln, & Harris, 1980; Crumpton et al., 1966; DiPietro et al., 1992; Faubel, 1989; Hallstrom & Noppa, 1981; Istvan et al., 1992; Moore et al., 1962; Palinkas et al., 1996; Ross, 1994). Whereas measures
that include both MD and AD somatic symptoms, but do not distinguish between the two, show more variable results.

The somatic symptoms associated with MD and AD are consistently associated with either negative or positive energy balance. Although MD is not complete in its distinction between bidirectional somatic symptoms (i.e. psychomotor agitation or retardation), it unidirectionally defines changes in appetite and sleep patterns (i.e. insomnia and hypophagia). Therefore, one would expect individuals with melancholic depression to be at increased risk for weight loss. Further, MD is associated with several demographic characteristics, including male gender and older age, that are consistent with populations that have demonstrated a negative relationship between weight and depression (Carpenter et al., 2000). In fact, it may be accurate to state that MD is protective for obesity among males.

In contrast, AD is only associated with symptoms that are consistent with a positive energy balance (i.e. hyperphagia, hypersomnia and psychomotor slowing). In addition, demographic characteristics associated with the AD subtype are also consistent with findings in the current literature (Carpenter et al., 2000; Haukkala & Uutela, 2000; Onyike et al., 2003). AD is up to four times more prevalent among female patients (Angst, Gamma, Sellaro, Zhang, & Merikangas, 2002; Benazzi, 1999; M. E. Thase, 1997). Obesity is also more common among women (Flegal et al., 2002). It is therefore not surprising that studies which failed to identify a relationship between obesity and depression in men, found a significant positive relationship among women
(DiPietro et al., 1992; Istvan et al., 1992). Therefore, differential prevalence of AD and MD among men and women may explain positive associations between weight and depression identified in women (DiPietro et al., 1992; Istvan et al., 1992) and negative associations identified in men (Silverstone, 1968; Simon, 1963). If AD and MD are distinct depressive syndromes, it is logical to hypothesize that AD, rather than general unipolar depression would be associated with obesity, whereas MD would be expected to be associated with decreases in weight and lower BMI.

Given that the prevalence and severity of individual symptoms may vary with age (Garber, Kriss, Koch, & Lindholm, 1988), it is necessary to examine the taxonomy of MD and AD among adolescents rather than extrapolate from the adult literature. The only study to examine the validity of adult symptoms of AD in adolescence has found only marginal associations among DSM-IV symptoms (Williamson et al., 2000). Two studies have examined the validity of the MD subtype among adolescents(Carmanico et al., 1998; Ryan et al., 1987), but they each identify different characteristics associated with MD. This suggests that a more accurate profile of depression in adolescents that includes unique class distinctions, and is not founded on research with adults, is necessary. Such a profile would improve identification of individuals most at risk for weight changes associated with a diagnosis of unipolar depression, and consequently identify those adolescents with depression who are at greatest risk for weight gain that would aid in tailoring treatments such that they improve both depression and weight outcomes in adolescents with reverse vegetative symptoms.
4.2 Study Aims and Hypotheses

This research sought to identify unique classes of depression with differential somatic symptom profiles in order to clarify the relationship between depression and weight in adolescents.

4.2.1 Study I

This study hypothesizes that latent classes of depression exist among adolescents that are consistent with established somatic symptom criteria for atypical and melancholic depression. This study will also seek to identify demographic characteristics, psychosocial co-morbidities and behavioral patterns associated with individual latent classes of depression.

4.2.2 Study II

This study also seeks to examine the relationship between depression class and BMI in a sample of adolescents diagnosed with major depression. It is hypothesized that depression class will predict BMI in this sample of adolescents. It is hypothesized that measures that assess both vegetative and reverse vegetative symptoms will show a stronger relationship between depression and BMI compared to those that do not, regardless of the inclusion of depression class as a covariate. It is also hypothesized that the relationship between depression and BMI will be stronger among classes associated with somatic symptoms, compared to classes not associated with somatic symptoms and that including class membership as a covariate will improve predictive model fit.
5. Methods

5.1 Participants

These hypotheses were tested in a sample of adolescents diagnosed with MDD enrolled in the Treatment for Adolescents with Depression Study (TADS; TADS Team, 2005). TADS is an NIMH-funded, multi-center, randomized control trial designed to evaluate the short and long term effectiveness of fluoxetine, cognitive behavioral therapy and their combination in a large treatment seeking cohort of 439 adolescents between the age of 12-17 years who met criteria for major depression. Patients were recruited from five sources: (1) site clinics; (2) schools and juvenile justice facilities; (3) primary care physicians; (4) other mental health providers; and (5) paid and public service advertisements in local media, including newspapers, radio, and TV.

Data was collected at a total of thirteen collection sites from a range of areas across the United States. Data for TADS was collected in several stages. Initial screening was conducted by telephone interview (gate A). This screen was followed by a clinic visit at which consent and assent were obtained prior to establishing study eligibility via the KSADS and CDRS-R (Gate B). Participants then returned between one and four weeks later for a final eligibility and baseline assessment prior to randomization to one of four treatments (Gate C). Data utilized for these analyses were obtained from baseline data collected at Gate B. Data from 550 participants were collected at gate B, however, 53 participants were missing data for weight, height or primary depression measures, resulting in a total N of 497. Data analyzed in this study includes 58 participants who
were not randomized to treatment at Gate C due to either refusal to continue participation prior to randomization or failure to continue to meet screening criteria for depression. These non-randomized participants were not significantly different from those who were randomized to treatment in regards to age, sex or socioeconomic status. They did however have significantly lower CDRS-R total scores (t=6.49, p<.0001). Because of this difference in CDRS-R scores, individuals who were not randomized to treatment may be more likely to be assigned membership to less severe latent classes compared to the randomized sample.

5.1.1 Inclusion Criteria

Participants were required to be between the age of 12 and 17 years (inclusive), enrolled in 6th through 12th grades (inclusive), must have a full scale IQ of at least 80 and must not be taking any antidepressants. They must have met requirements for a DSM-IV diagnosis of major depression at consent and baseline as well as a Children’s Depression Rating Scale-Revised (CDRS-R) score of 45 or higher at baseline. Depressed or irritable mood must have been present for at least 6 weeks prior to consent, accompanied by functional impairment in at least two of the following contexts: at home, at school or among peers. Participants and parents must have been capable of receiving outpatient treatment and sexually active female participants were required to agree to use contraception during study participation.
5.1.2 Exclusion Criteria

Exclusion criteria included current or previous diagnosis of bipolar disorder, severe conduct disorder, current substance abuse or dependence, thought disorders and pervasive developmental disorders. In addition, participants must not have been undergoing concurrent treatment with any psychotropic medication (except stable stimulant use for ADHD) or psychotherapy outside the study. They also must not have experienced more than one failure to respond to an adequate trial of a selective serotonin reuptake inhibitor (SSRI) and must not have had a poor response to clinical treatment with CBT for depression. Participants could not have an intolerance to fluoxetine or any confounding medical conditions. Patients could also be excluded for dangerousness to self or others if they had been hospitalized for dangerousness within the three months prior to consent or were deemed “high risk” by a cross-site panel. Finally, both parent and patients must be English speaking and a phone in the family home was required during the study (Treatment for Adolescents with Depression Study Team, 2005).

5.2 Measures

5.2.1 Demographics

Child psychosocial history was collected, including age, ethnicity, parental residential status in relation to the participant, and child and parent educational history were gathered via interview at Gate B.
5.2.2 Weight Status

5.2.2.1 BMI Percentile

Weight and height were assessed through clinician measurement at baseline and were used to calculate BMI for each individual. BMI scores were then transformed into a percentile score for age and gender. Although BMI has been shown to be a valid estimate of adiposity in children and adolescents compared with other body-composition screening indexes (Mei et al., 2002), it is not appropriate to use the adult BMI categories to interpret BMI numbers for children and teens. The BMI-for-age percentile is used to interpret the BMI number because BMI norms are both age-and sex-specific for children and teens. Age and sex must be considered in estimating adiposity as the amount of normal body fat changes with age and with gender. These criteria are different from those used to interpret BMI for adults, which do not take into account age or sex.

5.2.2.2 Obesity

For children, BMI is used to screen for overweight, at risk of overweight, or underweight. BMI is not a diagnostic tool in children and therefore, adult BMI categories should not be applied to children. For example, a child may have a high BMI for age and sex, but to determine if excess fat is a problem, a health care provider would need to perform further assessments. Consequently, in this study, consistent with the current literature, categorical weight status was delineated as <85th percentile, 85<sup>th</sup> to >95<sup>th</sup>
percentile and ≥95th percentile of BMI for age and gender (Himes & Dietz, 1994; Barlow & Dietz, 1998)

5.2.3 Pubertal Development

The Tanner Staging System (Dorn, Sueman, Nottelman, & Inoff-Germain, 1990) was used to rate sexual maturity and physical development. The Tanner ratings were obtained via self-report supplemented by the clinician’s impression based on the overall presentation of the participant. The adolescent was asked to self-rate development using a set of pictures depicting males or females at various stages of sexual development. The majority of girls have completed their final “growth spurt” once they have reached Tanner stage 3, but smaller gains in height are common through Tanner stage 4. Boys typical show greatest gains in height at Tanner stage 4 and may continue growing 1-2 years post puberty.

5.2.4 Measures of Adolescent Depression

Although parent measures, including parent responses on the CDRS-R, were collected as part of the TADS protocol, adolescent report of symptomatology was used as self-ratings have proven to be especially useful measures of symptoms of internalizing disorders (Loeber, Green, Lahey, & Stouthamer-Loeber, 1989). It was decided not to include parent ratings of child symptoms to avoid the introduction of bias for behavioral over mood symptoms in the final groups (i.e. the analysis would be biased to identify classes that were unbalanced and source specific as a corresponding second informant would not be available to provide an equally valid report of
internalizing symptoms). In addition, correlational analyses of parent and child measures showed inconsistent associations between parent and child report of psychosocial symptoms. For example, although all adolescent self-report measures of depression showed strong associations between measures, comparison of adolescent measures with parent report of adolescent depression on the CDRS-R showed moderate associations, with effect sizes no stronger than $r = 0.65$, suggesting meaningful differences between child and parent report. In addition, only child report was available for the comparative depression measure used in study 2 (RADS), therefore use of only child responses maintained consistency. Thus, only adolescent report measures of psychological symptoms were used in these analyses. This is different from previous publications from this dataset, which used depression ratings reconciled by a clinician for differences between parent and child responses on the CDRS-R.

5.2.4.1 Children’s Depression Rating Scale Revised (CDRS-R; Poznanski & Mokros, 1996)

The CDRS-R is a well-validated clinical interview tool that has received wide use as the primary scalar dependent measure in treatment studies for depression in children. It is used to assess children ages 6 – 18, is modeled after the Hamilton Rating Scale for Depression and can typically be administered in 15-20 minutes. The CDRS-R has good reliability, with interrater correlations ranging from 0.74–0.96 and test–retest correlations ranging from (0.80–0.96), as well as sound internal consistency ($\alpha=0.70$). The CDRS-R assesses 17 symptom areas relevant to pediatric Major Depression: impaired
schoolwork, difficulty having fun, social withdrawal, appetite disturbance, sleep disturbance, excessive fatigue, physical complaints, irritability, excessive guilt, low self-esteem, depressed feelings, morbid ideas, suicidal ideas, excessive weeping, depressed facial affect, listless speech, and hypoactivity. Responses to 14 items are given on a 7-point self or parent-report scale. Differences between adolescent and parent report can then be reconciled by a clinician resulting in a separate score reflecting the responses of both informants. The final 3 items (items 15-17) on this scale are clinician ratings on a five-point scale based on observation of the child. Only child rating and clinician observation ratings were used in this study. Scores range from 17-113. A score of 45 or greater indicates clinically significant symptoms of depression. For the purposes of latent class analysis, information from two ancillary items that provide more detailed information about appetitive change and type of insomnia were used to create five additional dichotomous items indicating presence or absence of hyperphagia, hypophagia, initial insomnia, intermediate insomnia and terminal insomnia. These items were only used for the purposes of LCA and were not used for any other analyses.

5.2.4.2 Clinical Global Impression-Severity (CGI-S; Guy, 2000)

The CGI is a three-item scale used to assess treatment response in psychiatric patients. They are: Severity of Illness; Global Improvement; Efficacy Index. Item 1 is rated on a seven-point scale (1=normal to 7=extremely ill); item 2 on a seven-point scale (1=very much improved to 7=very much worse); and item 3 on a four-point scale (from 'none' to 'outweighs therapeutic effect'). Severity of Illness is the item of primary interest
for the current analyses. It requires the clinician to rate the severity of the patient’s illness at the time of assessment, relative to the clinician’s past experience with patients who have the same diagnosis. Considering total clinical experience, a patient is assessed on severity of mental illness at the time of rating according to: normal (not at all ill); borderline mentally ill; mildly ill; moderately ill; markedly ill; severely ill; or extremely ill. Clinician ratings were informed by an independent evaluator manual that provided anchors, including CDRS-R scores for different CGI-S ratings.

5.2.4.3 Reynolds Adolescent Depression Scale (RADS-2; Reynolds, 1987b)

This self-report scale for children ages 11-18 assess four basic categories of depressive symptoms: negative/sad mood, depressed/withdrawn emotions, negative self-esteem, and physical manifestations. Reliability coefficients for the RADS range from 0.91-0.94, with total sample alpha reliability of 0.92 and split-half reliability of 0.91. Six week and 3-month test-retest coefficients are 0.80 and 0.79, respectively. Scores range from 30-120 on this 30-item 4-point scale. The measure typically takes about 10 minutes to complete. Interpretation of the subscales is based on both the nature of the depression domain and the item content of the subscale.

5.2.4.4 Suicidal Ideation Questionnaire Grades 7-9 (SIQ-Jr; Reynolds, 1987a)

The SIQ is a companion instrument to the RADS for use in assessing suicidal ideation. SIQ-JR has 10 items with responses on a 7-point scale. Scores range from 0 to 60. The SIQ-JR has high reliability ($\alpha=0.94$) and validity.

5.2.4.5 Beck Hopelessness Scale (BHS; A. T. Beck & Steer, 1988)
The BHS is a 20-item self-report true/false measure of hopelessness, which has been found to be a predictor of suicidal risk. Scores range from 0 to 20. The internal reliability coefficients are high (α=0.82 - 0.93) and the test-retest reliability coefficients are modest (0.69 after one week and 0.66 after six weeks).

5.2.5 Measures of Co-Morbid Adolescent Psychopathology

5.2.5.1 Multidimensional Anxiety Scale for Children (MASC; March, Parker, Sullivan, Stallings, & Conners, 1997)

The MASC is a 39-item 4-point self-report instrument used to assess the child’s experience of anxiety symptoms. It requires approximately 15 minutes to complete. Total scale scores range from 0 to 117. In addition to the Anxiety Disorders Index, the Total Anxiety Index and the Inconsistency Index, scoring results in a total of 4 subscales: the Physical Symptoms Scale, the Social Anxiety Scale, the Harm Avoidance Scale, and the Separation /Panic Scale. Internal reliability for the MASC total score is 0.9 and ranges from 0.6 to 0.85 for the subscales. Test-retest reliability for the total score at 3 weeks and 3 months is 0.785 and 0.933 respectively.

5.2.5.2 Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire (PQ-LES-Q; Endicott, Nee, Yang, Wohlberg, 2006)

A pediatric adaptation of Jean Endicott's QLES-Q, the most commonly used, well-validated quality of life scale found in the adult treatment outcome literature, was used to assess general quality of life. This 5-point 15-item self-report measure assesses the degree of enjoyment and satisfaction experienced by subjects in various areas of daily functioning over the past week. Scores range from 15 to 75. Internal consistency
coefficients at screening, baseline, and endpoint were high (0.87, 0.90, 0.89, respectively) as was the 1-week test-retest intraclass correlation coefficient of reliability (0.78).

5.2.5.3 Conners’ Wells’ Adolescent Self-report Scale (CASS:L; Conners et al., 1997)
The CASS:L is a child report measure of family, emotional and cognitive difficulties normed on a representative sample of 2,000 12-18 year olds. It contains 102 4-point (not true, just a little true, pretty much true, and very much true) self-report items. Subscale scores are transformed into t-scores. The CASS has validated and reliable factors in six domains: family problems, emotional problems, conduct problems, cognitive problems, anger control problems, and hyperactivity. Coefficient alphas for the measure range from 0.83 to 0.92. Median test-retest reliability for the six domains was 0.86.

5.3 Analysis
All data analysis was conducted using SAS version 9.0. Bivariate analyses were conducted using chi square tests for categorical data and paired t-tests for continuous data by gender and BMI group. Spearman non-parametric correlation coefficients were calculated for continuous data. In cases where chi square analyses resulted in cells with fewer than five members, Fisher’s exact test was used to test for significant differences between groups. Analyses examining the relationship between depression score on the CDRS-R and RADS, depression class and BMI percentile included correlation, chi square, linear regression and multivariate analyses. The Holms-Bonferroni correction for multiple comparisons was used to reduce type I error for all hypothesis driven comparisons.
Body mass index percentiles and BMI z-scores (zBMI) were computed using the SAS program `gc-calculate-BIV.sas` (CDC, 2005). The program was designed to easily generate a dataset that contains indices of the anthropometric status of children from birth to 20 years of age based on the 2000 CDC growth charts. This version of the SAS program includes identifying outlier observations or observations that are considered to be "biologically implausible values (BIVs).

Subsequent to the calculation of simple statistics to characterize the sample, exploratory Latent Class Analysis (LCA) was conducted using the Proc LCA statement developed by the Methodology Center (Lanza, Collins, Lemmon, Schafer, 2007). LCA is a person, rather than symptom focused statistical technique for identifying mutually exclusive classes of symptoms. It provides symptom endorsement probabilities within each class. Conceptually similar to cluster analysis, LCA assumes an underlying latent variable that determines an individual’s class membership. It uses categorical variables as indicator variables and determines the optimal solution by comparison of fit statistics. The ultimate goal of LCA is to achieve maximum homogeneity within classes and maximum differentiation between classes. Thus, LCA groups individuals into categories on the basis of shared characteristics that distinguish members of one group from members of another group. Each class gets a weight, that is, the proportion of persons belonging to that class, and each class has its own class specific item probabilities, that is, the probability of endorsing each of the items. Finally, individual class assignment is
identified using probability statistics generated by the LCA program indicating probability of membership for each of the identified classes.

Each model was estimated by stepwise addition of classes, until the model fitted the data best, in order to obtain an optimal class-solution. The stability of each model was examined by using different sets of starting values to prevent solutions based on a local maximum in iteration processes. Once a stable model was identified, values of the BIC of each model were compared, and the model with lowest BIC was preferred. The BIC is a relative (with respect to the corresponding numbers for other models) fit measure for parametric models that compensates for the number of parameters in the model, thereby decreasing the likelihood of overparameterization (Kass & Wasserman, 1995). Smaller values of BIC indicate better model fit.

Latent class analysis was conducted exclusively using items from the CDRS-R in order to eliminate any repetition of symptoms. Previous research in this area using items from both the BDI and K-SADS (Ambrosini et al., 2002; Williamson et al., 2000) resulted in classes containing items from one measure or the other. Hence, one might argue that it is depression as assessed by K-SADS versus the BDI, and not subtypes of depression per se, that are the categorical constructs being identified. Therefore, it was decided that the use of a single measure of depression would result in the most parsimonious solution.

In order to simplify interpretation and accommodate the requirements of LCA, responses to items on the CDRS-R were dichotomized into not present (responses of 1, 2,
or 3) and present (responses >3). In addition, items 4 and 5 on the CDRS-R, which assess for any changes in sleep and appetite, were eliminated in favor of supplemental items that specifically assess for type of sleep and appetite disturbance resulting in 5 additional dichotomous items indicating presence or absence of hyperphagia, hypophagia, initial insomnia, intermediate insomnia and terminal insomnia. These items were only used for the purposes of LCA. It should be noted that by exclusively using items from the CDRS-R, the analyses were unable to include leaden paralysis, psychomotor agitation or hypersomnia as class related symptoms, as they are not specifically assessed via this measure. However, although less specific in nature, items assessing for excessive fatigue, hypoactivity and listless speech were included in LCA analyses and are consistent with leaden paralysis. Research in youth has demonstrated higher prevalence of these anergic symptoms in an AD population (Silverstein et al., 2006). In addition, initial insomnia is not antithetical to hypersomnia, as disrupted sleep patterns from oversleeping during the day may result in initial insomnia at bedtime. In fact a study of youth aged 11-22 showed that the proportion of respondents meeting criteria for AD who experienced difficulty falling asleep, defined as wakefulness of at least 30 minutes after bedtime, was double that of Non-AD youth (Silverstein et al., 2006). However, intermediate and terminal insomnia are not consistent with hypersomnia as they are defined as waking from sleep prior to acquiring sufficient sleep. Thus, we would expect initial insomnia but not intermediate or terminal insomnia in classes that are consistent with AD. Although the data does not allow for direct
assessment of the association of the fore mentioned unavailable symptoms with particular classes of depression, analyses will indicate symptom patterns that are either consistent or inconsistent with these symptoms.
6. Results

6.1 Characteristics of the Sample

6.1.1 Demographic Characteristics

Data from a total of 496 youths (231 males and 265 females) were analyzed. Average age of the sample was 14.56±1.56. In regard to pubertal status, 78.8% were identified as post pubertal (Tanner stage 4 or 5). Thus, a large majority of the sample had either completed or nearly completed puberty. 46.53% of the sample had completed the 9th grade. The majority of the sample was Caucasian (70.36%), followed by African American (16.53%) and Hispanic (8.47%). Less than 5% of the sample self identified as Asian, Native American, Pacific Islander or other and so were combined into an “other” group.

In regards to family demographics, only 2.19% of the sample were only children, with the majority having one, (25.71%), two (32.6%) and three (20.69%) full or half siblings. The majority of adolescents had at least one parent who was married (70.88%). The majority of parents were or had been married to each other (83.03%). The majority of families had an annual income between $40,000 - $75,000 and nearly all parents had earned a high school diploma or equivalent. Average age of fathers was 42.77±7.40. Average age of mothers was 45.34±8.29. Table 1 displays the overall adolescent socio demographics by gender. Bivariate $X^2$, Fisher’s Exact and paired t-test analyses revealed no significant differences in gender for any adolescent or family demographic variables except BMI z-score and academic performance.
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<th>Female</th>
<th>P Value</th>
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<td>N = 265</td>
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<td>14.56</td>
<td>14.55</td>
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<td>1.51</td>
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<td>8.07</td>
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<td><strong>SD</strong></td>
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<td><strong>Tanner 3</strong></td>
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<td>32 (12.75%)</td>
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<td>109 (50.46%)</td>
<td>121 (48.21%)</td>
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<td><strong>Tanner 5</strong></td>
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<td>53 (24.54%)</td>
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<td>97 (23.26%)</td>
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<tr>
<td>Average</td>
<td>134 (32.13%)</td>
<td>59 (31.22%)</td>
<td>75 (32.89%)</td>
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</tr>
<tr>
<td>Below Average</td>
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<td>95 (50.26%)</td>
<td>75 (32.89%)</td>
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<td></td>
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<td>4th or 5th</td>
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<td>9 (3.95%)</td>
<td>8 (3.05%)</td>
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<td>6th</td>
<td>65 (13.27%)</td>
<td>30 (13.16%)</td>
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<td>7th</td>
<td>85 (17.35%)</td>
<td>40 (17.54%)</td>
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<td>8th</td>
<td>95 (19.39%)</td>
<td>51 (22.37%)</td>
<td>44 (16.79%)</td>
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<td>9th</td>
<td>103 (21.02%)</td>
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<td>10th</td>
<td>85 (17.35%)</td>
<td>39 (17.11%)</td>
<td>46 (17.56%)</td>
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<td>11th or 12th</td>
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<tr>
<td></td>
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<td><strong>Family income (NS)</strong></td>
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<td>$0-$19,999</td>
<td>57 (13.32%)</td>
<td>20 (10.15%)</td>
<td>37 (16.02%)</td>
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<tr>
<td>$20,000-$39,999</td>
<td>111 (25.93%)</td>
<td>54 (27.41%)</td>
<td>57 (24.68%)</td>
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<tr>
<td>$40,000-$75,999</td>
<td>155 (36.21%)</td>
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<td>84 (36.36%)</td>
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<td>$75,000-$99,999</td>
<td>43 (10.05%)</td>
<td>20 (10.15%)</td>
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<td>$100,000+</td>
<td>62 (14.49%)</td>
<td>32 (16.24%)</td>
<td>30 (12.99%)</td>
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<td><strong>Father’s education level (NS)</strong></td>
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<tr>
<td>Less Than High School</td>
<td>27 (7.38%)</td>
<td>8 (4.73%)</td>
<td>19 (9.64%)</td>
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</tr>
<tr>
<td>High School or Equiv.</td>
<td>150 (40.98%)</td>
<td>68 (40.24%)</td>
<td>82 (41.62%)</td>
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<tr>
<td>Some College</td>
<td>81 (22.13%)</td>
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<td>Bachelor’s Degree</td>
<td>62 (16.94%)</td>
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<tr>
<td>Graduate Degree</td>
<td>46 (12.57%)</td>
<td>24 (14.20%)</td>
<td>22 (11.17%)</td>
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<td><strong>Mother’s education level (NS)</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Less Than High School</td>
<td>28 (5.91%)</td>
<td>7 (3.23%)</td>
<td>21 (8.17%)</td>
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<tr>
<td>High School or Equiv.</td>
<td>174 (36.71%)</td>
<td>85 (39.17%)</td>
<td>89 (34.63%)</td>
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<tr>
<td>Some College</td>
<td>134 (28.27%)</td>
<td>56 (25.81%)</td>
<td>78 (30.35%)</td>
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<tr>
<td>Bachelor’s Degree</td>
<td>96 (20.25%)</td>
<td>47 (21.66%)</td>
<td>49 (19.07%)</td>
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<tr>
<td>Graduate Degree</td>
<td>42 (8.86%)</td>
<td>22 (10.14%)</td>
<td>20 (7.78%)</td>
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<td><strong>Parent marital status (NS)</strong></td>
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<td>Parents never married</td>
<td>83 (16.97%)</td>
<td>32 (14.04%)</td>
<td>51 (19.54%)</td>
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<tr>
<td>Parents married</td>
<td>173 (41.49%)</td>
<td>98 (42.98%)</td>
<td>99 (37.93%)</td>
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</tr>
<tr>
<td>Parents legally separated</td>
<td>13 (3.12%)</td>
<td>4 (1.75%)</td>
<td>9 (3.45%)</td>
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<tr>
<td>Parents are divorced</td>
<td>141 (33.81%)</td>
<td>80 (35.09%)</td>
<td>85 (32.57%)</td>
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<tr>
<td>One or both deceased</td>
<td>23 (5.52%)</td>
<td>14 (6.14%)</td>
<td>17 (6.51%)</td>
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</tr>
<tr>
<td>Father married another</td>
<td>77 (18.83%)</td>
<td>35 (18.72%)</td>
<td>42 (18.92%)</td>
<td></td>
</tr>
<tr>
<td>Mother married another</td>
<td>80 (19.18%)</td>
<td>36 (19.05%)</td>
<td>44 (19.30%)</td>
<td></td>
</tr>
</tbody>
</table>

* Fisher’s Exact Test
BMI percentile for age and gender was in the normal range (weight up to 85th percentile) for 54.23% of the sample, the 85th-95th percentile for 16.33% of the sample and at or above the 95th percentile for 29.44% of the sample. This is notably higher than rates found in US epidemiological studies which show 17.4% prevalence of overweight (BMI above 95 percentile) among youths between the ages of 12 to 19 years (Ogden, Flegal, Carroll, & Johnson, 2002a). Less than 2% of the sample met criteria for the underweight range (<5th percentile). Therefore, comparisons of underweight to other weight categories could not be accomplished. Table 2 displays the overall socio demographics by BMI group (<85th percentile, 85th-95th percentile and >95th percentile). No significant differences were identified between the three BMI groups. BMI z-score was significantly associated with adolescent age, (r=-0.14. p<0.005), maternal age (r=-0.12, p<0.01), maternal education level (r=-0.13, p<0.0001), and paternal education level (r=-0.22, p<0.0001), but not paternal age or family income.

Table 2
Adolescent Demographic Characteristics by BMI Class

<table>
<thead>
<tr>
<th>Demographic variable</th>
<th>&lt; 85th %ile (n = 269)</th>
<th>85th – 95th %ile (n = 81)</th>
<th>≥95th %ile (n = 146)</th>
<th>P Value</th>
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<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
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<td>Age</td>
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<td>14.12b</td>
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<td>Gender (NS)</td>
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<tr>
<td>Male</td>
<td>128 (55.41%)</td>
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<tr>
<td>Female</td>
<td>141 (53.21%)</td>
<td>44 (16.60%)</td>
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<td>Pubertal status (NS)</td>
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<td></td>
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</tr>
<tr>
<td>Tanner 1</td>
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<tr>
<td>Tanner 2</td>
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</tr>
<tr>
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<table>
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<td>Other</td>
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<td>27.79%</td>
</tr>
<tr>
<td></td>
<td>35.37%</td>
</tr>
<tr>
<td></td>
<td>35.71%</td>
</tr>
<tr>
<td></td>
<td>21.74%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Grades (NS)</th>
<th>0.26</th>
</tr>
</thead>
<tbody>
<tr>
<td>Better than Average</td>
<td>61</td>
</tr>
<tr>
<td>Average</td>
<td>68</td>
</tr>
<tr>
<td>Below Average</td>
<td>88</td>
</tr>
<tr>
<td></td>
<td>26.99%</td>
</tr>
<tr>
<td></td>
<td>30.09%</td>
</tr>
<tr>
<td></td>
<td>38.94%</td>
</tr>
<tr>
<td></td>
<td>13.70%</td>
</tr>
<tr>
<td></td>
<td>28.77%</td>
</tr>
<tr>
<td></td>
<td>52.05%</td>
</tr>
<tr>
<td></td>
<td>22.03%</td>
</tr>
<tr>
<td></td>
<td>38.14%</td>
</tr>
<tr>
<td></td>
<td>37.29%</td>
</tr>
</tbody>
</table>

Fisher’s Exact Test

6.1.2 Adolescent Psychological Characteristics

Means and standard deviations for psychosocial measures are presented in tables 3 and 4. Paired t-test analyses identified several significant differences among psychiatric variables for gender. Female adolescents endorsed greater symptomatology on the CDRS-R (56.23 vs. 50.04), the RADS (81.94 vs. 75.78), the BHS (10.23 vs. 9.34), the SIQ (27.33 vs.17.73) and the MASC (53.18 vs. 43.57). Means from additional psychosocial measures are available in the appendices. Symptom endorsement on the CDRS-R, were
as follows: Impaired schoolwork (79.44%), difficulty having fun (82.66%), social withdrawal (65.52%), excessive fatigue (78.63%), physical complaints (41.33%), irritability (78.63%), excessive guilt (26.01%), low self-esteem (75.60%), depressed feelings (79.64%), morbid ideation (25.40%), suicidal ideation (17.94%), excessive weeping (33.67%), depressed facial affect (70.97%), listless speech (35.69%), hypoactivity (47.18%), initial insomnia (68.15%), intermediate insomnia (27.22%), terminal insomnia (15.12%), increased appetite (26.81%), and decreased appetite (45.97%).

### Table 3
**Adolescent Psychological Characteristics by Gender**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Total (N = 496)</th>
<th>Male (n = 231)</th>
<th>Female (n = 265)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>CDRS-R</td>
<td>53.89</td>
<td>13.70</td>
<td>49.95</td>
<td>12.78</td>
</tr>
<tr>
<td>RADS</td>
<td>78.86</td>
<td>14.49</td>
<td>73.81</td>
<td>14.94</td>
</tr>
<tr>
<td>BHS (NS)</td>
<td>9.83</td>
<td>5.57</td>
<td>9.34</td>
<td>5.69</td>
</tr>
<tr>
<td>SIQ</td>
<td>23.23</td>
<td>22.16</td>
<td>18.20</td>
<td>20.24</td>
</tr>
<tr>
<td>PQ-LES-Q</td>
<td>43.21</td>
<td>9.00</td>
<td>45.22</td>
<td>9.46</td>
</tr>
<tr>
<td>MASC total</td>
<td>48.78</td>
<td>17.54</td>
<td>43.61</td>
<td>15.60</td>
</tr>
<tr>
<td>Perfectionism</td>
<td>46.38</td>
<td>10.57</td>
<td>46.44</td>
<td>10.03</td>
</tr>
<tr>
<td>Somatization</td>
<td>53.04</td>
<td>10.71</td>
<td>52.05</td>
<td>10.80</td>
</tr>
<tr>
<td>Physical Symptom</td>
<td>56.00</td>
<td>10.75</td>
<td>54.91</td>
<td>10.93</td>
</tr>
<tr>
<td>Separation / Panic</td>
<td>52.63</td>
<td>11.91</td>
<td>51.08</td>
<td>10.08</td>
</tr>
<tr>
<td>Humiliation / Rejection</td>
<td>58.65</td>
<td>12.59</td>
<td>58.95</td>
<td>12.56</td>
</tr>
<tr>
<td>Social Anxiety</td>
<td>59.24</td>
<td>12.72</td>
<td>59.51</td>
<td>12.18</td>
</tr>
</tbody>
</table>

*Note: CDRS-R = Children’s Depression Rating Scale Revised, RADS = Reynold’s Adolescent Depression Rating Scale, BHS = Beck Hopelessness Scale, SIQ = Suicidal Ideation Questionnaires Jr, PQ-LES-Q = Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire, MASC = Multidimensional Anxiety Scale for Children*
No significant differences were identified between BMI categories and psychosocial measures except for the BHS. Adolescents who were overweight scored higher on the BHS compared to both the normal weight and obese samples (See table 4). Symptom level analyses for somatic symptoms on the CDRS-R most likely to be related to BMI were not significant for hypoactivity, initial insomnia, intermediate insomnia, terminal insomnia or hypophagia. zBMI and endorsement of hyperphagia were significantly associated (t=3.85, p<0.0001).

### Table 4

<table>
<thead>
<tr>
<th>Adolescent Psychological Characteristics by BMI Class</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;85th %ile</td>
</tr>
<tr>
<td>n = 261</td>
</tr>
<tr>
<td>Mean</td>
</tr>
<tr>
<td>--------</td>
</tr>
<tr>
<td>CDRS -R</td>
</tr>
<tr>
<td>RADS</td>
</tr>
<tr>
<td>BHS ab</td>
</tr>
<tr>
<td>SIQ</td>
</tr>
<tr>
<td>MASC</td>
</tr>
<tr>
<td>PQLQ</td>
</tr>
</tbody>
</table>

*Note:* Means with different superscripts are significantly different

### 6.1.3 Associations with Depression Measures

All measures of depression (CDRS-R, RADS, BHS, and SIQ) were significantly intercorrelated, with r values ranging from 0.35 between BHS and CDRS-R and 0.59 between RADS and SIQ. The r value for the correlation between the two primary measures of depression, CDRS-R and RADS, was 0.56 (p<0.0001). Elevated CDRS-R
scores were associated with decreased adolescent reported quality of life ($r=-0.48$, $p<0.0001$), increased physical complaints ($r=0.40$, $p<0.0001$) and elevated MASC total scores ($r=0.27$, $p<0.0001$), as well as elevated MASC humiliation/rejection ($r=0.14$, $p<0.005$), performance fears ($r=0.12$, $p<0.01$), social anxiety ($r=0.14$, $p<0.005$), and separation/panic ($r=0.13$, $p<0.005$) subscales. In addition, significant ANOVA analysis of the relationship between pubertal status and CDRS-R scores revealed significantly increasing CDRS-R scores for each level of pubertal development ($f=2.79$, $df=4$, $p=0.03$). Significant associations between the RADS and psychosocial variables paralleled those of the CDRS-R.

### 6.2 Study I

#### 6.2.1 Latent Class Analysis

Exploratory LCA revealed that a six-class solution fit the data best. The six class solution resulted in the lowest BIC value and was thus selected as the most parsimonious model. The values of BIC for of a 1 – 7 class solution derived from exploratory LCA are presented in Figure 1. Conditional response probabilities for each symptom within each of the six classes are presented in Table 6. Values greater than 0.5 indicate a greater than 50% chance that respondents belonging to that class will endorse that item.
Figure 1 BIC Fit Statistics for Models With 1-7 Classes
Classes were both phenotypic and dimensional in character, with each unique phenotypic classes identified based partly on differences in somatic, especially phagic, symptoms. Phagic symptoms had an extremely low prevalence in classes 1 and 2. Class 1 was termed “Mild” as no items on the CDRS-R had a greater than 50% chance of endorsement. Participants in this class had a near equal probability of endorsing hypophagia or no phagic symptoms at all. Class 2 was termed “Moderate” as it showed moderate prevalence of most symptoms with no distinguishing low or high prevalence items. Class 2 had a 0% probability of endorsing any phagic symptoms. There was a 100%) probability of hypophagia in Classes 3 (Moderate with Hypophagia), and 5 (Melancholic), with class 5 characterized by comparatively elevated symptom probabilities. There was a 100% probability of hyperphagia in classes 4 (Moderate with Hyperphagia) and 6 (Atypical), with class 6 characterized by a greater number of elevated symptom probabilities.
<table>
<thead>
<tr>
<th>Depression Class Loadings</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.27%)</td>
<td>21.22%)</td>
<td>23.17%)</td>
<td>11.22%)</td>
<td>20.49%)</td>
<td>14.63%)</td>
<td></td>
</tr>
<tr>
<td>Depression Feelings</td>
<td>0.0397</td>
<td>0.8679</td>
<td>0.8222</td>
<td>0.9092</td>
<td>1.0000</td>
<td>0.9237</td>
</tr>
<tr>
<td>Anhedonia</td>
<td>0.1748</td>
<td>0.9369</td>
<td>0.8623</td>
<td>0.8863</td>
<td>0.9433</td>
<td>0.9248</td>
</tr>
<tr>
<td>Excessive Fatigue</td>
<td>0.1047</td>
<td>0.8518</td>
<td>0.7933</td>
<td>0.9176</td>
<td>0.9405</td>
<td>0.8537</td>
</tr>
<tr>
<td>Schoolwork</td>
<td>0.3632</td>
<td>0.8336</td>
<td>0.8927</td>
<td>0.7987</td>
<td>0.8564</td>
<td>0.8025</td>
</tr>
<tr>
<td>Low Self-Esteem</td>
<td>0.0977</td>
<td>0.8419</td>
<td>0.6683</td>
<td>0.9538</td>
<td>0.9741</td>
<td>0.8113</td>
</tr>
<tr>
<td>Irritability</td>
<td>0.3605</td>
<td>0.8077</td>
<td>0.7285</td>
<td>0.8974</td>
<td>0.9839</td>
<td>0.7374</td>
</tr>
<tr>
<td>Social Withdrawal</td>
<td>0.2025</td>
<td>0.6643</td>
<td>0.6963</td>
<td>0.6480</td>
<td>0.8429</td>
<td>0.6672</td>
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<tr>
<td>Depression Facial Affect</td>
<td>0.4210</td>
<td>0.6990</td>
<td>0.7644</td>
<td>0.3863</td>
<td>0.7870</td>
<td>0.9834</td>
</tr>
<tr>
<td>Hypoactivity</td>
<td>0.2638</td>
<td>0.5028</td>
<td>0.5537</td>
<td>0.0000</td>
<td>0.4307</td>
<td>0.9185</td>
</tr>
<tr>
<td>Physical Complaints</td>
<td>0.0340</td>
<td>0.3803</td>
<td>0.3457</td>
<td>0.5970</td>
<td>0.6656</td>
<td>0.3629</td>
</tr>
<tr>
<td>Excessive Weeping</td>
<td>0.0254</td>
<td>0.2765</td>
<td>0.0849</td>
<td>0.3580</td>
<td>0.7189</td>
<td>0.4419</td>
</tr>
</tbody>
</table>
Table 4 Continued

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Class 1</th>
<th>Class 2</th>
<th>Class 3</th>
<th>Class 4</th>
<th>Class 5</th>
<th>Class 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Listless speech</td>
<td>0.1671</td>
<td>0.3762</td>
<td>0.3986</td>
<td>0.0000</td>
<td>0.3499</td>
<td>0.6268</td>
</tr>
<tr>
<td>Excessive Guilt</td>
<td>0.1302</td>
<td>0.2073</td>
<td>0.1656</td>
<td>0.2655</td>
<td>0.5385</td>
<td>0.1949</td>
</tr>
<tr>
<td>Morbid Ideation</td>
<td>0.0000</td>
<td>0.2649</td>
<td>0.0577</td>
<td>0.3727</td>
<td>0.4964</td>
<td>0.2854</td>
</tr>
<tr>
<td>Suicidal Ideation</td>
<td>0.0253</td>
<td>0.2073</td>
<td>0.0190</td>
<td>0.2159</td>
<td>0.4275</td>
<td>0.1703</td>
</tr>
<tr>
<td>Initial Insomnia</td>
<td>0.4904</td>
<td>0.7342</td>
<td>0.6484</td>
<td>0.7490</td>
<td>0.7569</td>
<td>0.6602</td>
</tr>
<tr>
<td>Intermediate Insomnia</td>
<td>0.1270</td>
<td>0.1730</td>
<td>0.1589</td>
<td>0.2590</td>
<td>0.4345</td>
<td>0.3500</td>
</tr>
<tr>
<td>Terminal Insomnia</td>
<td>0.1008</td>
<td>0.1381</td>
<td>0.0961</td>
<td>0.0150</td>
<td>0.2495</td>
<td>0.1839</td>
</tr>
<tr>
<td>Hyperphagia</td>
<td>0.2368</td>
<td>0.0000</td>
<td>0.0000</td>
<td>1.0000</td>
<td>0.0000</td>
<td>1.0000</td>
</tr>
<tr>
<td>Hypophagia</td>
<td>0.4040</td>
<td>0.0000</td>
<td>1.0000</td>
<td>0.0000</td>
<td>1.0000</td>
<td>0.0000</td>
</tr>
</tbody>
</table>

Note: Class loadings are equivalent to percent of individuals endorsing each symptom within each depression class. Percent endorsement can be obtained by multiplying class loadings by 100.

Although classes 3 and 4 were distinct based on phagic symptoms (i.e. only hypo or hyperphagia), their remaining symptom profiles did not parallel the profile of their respective more severe phagic classes. In fact, upon visual inspection, Moderate with Hypophagia more closely paralleled the symptom profile of the Atypical class and Moderate with Hyperphagia more closely paralleled the symptom profile of the Melancholic class. In addition, the symptom profile of class 2 (Moderate) displayed similarly elevated symptom occurrence when compared to both the moderate phagic classes suggesting that classes 2, 3 and 4 are more closely related than class 3 and 5 or class 4 and 6. Comparisons of of the Moderate Hyperphagic and Hypophagic classes
with the Moderate, Atypical and Melancholic classes are presented in figures 2, 3 and 4. Figures displaying the profiles of the two moderate phagic classes with their phagically antithetical severe classes are available in the appendices. Multiple comparisons were corrected for using the Holmes-Bonferroni correction.

Figure 2 Comparison of Classes with Hyperphagic Symptomatology (Classes 4 and 6)
Figure 3 Comparison of Classes with Hypophagic Symptomatology (Classes 3 and 5)

Figure 4 Comparison of Classes with Moderate Symptomatology (Classes 3, 4 and 2)
In order to support the assignment of dimensional descriptors to each class, severity ratings were checked using independent t-test analysis, to determine if CDRS-R total scores and CGIS ratings were significantly different between classes. Results are presented in Figures 5 and 6. Class 5 (Melancholic) produced the highest severity between all classes. Class 6 (Atypical) produced the second highest severity. Class 1 (Mild) severity was significantly lower when compared to all classes. Additional comparisons revealed no significant differences in severity between the moderate classes (2, 3 and 4). Comparisons using the CGIS did not result in any significant findings, however the overall pattern of results is consistent with the pattern noted in the CDRS-R comparisons. Overall, examination of levels of severity between classes was consistent with severity descriptors assigned based on the latent class analysis.

Figure 5 Child Depression Rating Scale by Depression Class
6.2.2 Associations Between Depressive Class and Demographic Variables

Other measures of psychopathology, including additional depression related variables, were used to further examine the characteristics of the six latent subtypes. Comparisons of categorical and quantitative variables across classes were performed using chi square and correlation analyses to identify associations between type of depressive class and demographic variables. Comparisons of race were conducted with African American, Hispanic and Other classes collapsed, as \( \chi^2 \) analysis using all four race groups resulted in 0 count cells. Overall chi square for latent class and gender (\( \chi^2 = 37.26, \ p<.0001 \)) as well as latent class and race (\( \chi^2 = 28.27, \ p<.0001 \)) were significant. No
significant differences were found for gender for individual classes after correction for multiple comparisons. In regard to race, the Mild and MD classes had significantly fewer Caucasians. This is not consistent with data from adults, which indicated that Caucasian race is more common among AD and MD depression subtypes. No associations were found for family income, parental level of education, parent marital status, or number of siblings. Chi square analysis for BMI group and latent class was significant when comparing individuals in the ≥95th percentile to those <95th percentile ($\chi^2 = 28.27, p<.0001$). Chi square analysis for latent class and all three BMI groups ($\chi^2 = 28.27, p<.0001$) lost significance after Holms-Bonferroni correction (See Figure 7).

Table 6

| Demographic Characteristics by Depression Class |
|-----------------|----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | 1              | 2              | 3               | 4               | 5               | 6               |                 |
| Moderate        | 34.21          | 49.43          | 38.95           | 73.91           | 72.62           | 65.00           |
| Moderate w/ Hypophagia | 50.00 b       | 77.01 a        | 70.53 b         | 86.96 c         | 82.14 b         | 55.00 a         |
| Moderate w/ Hyperphagia | 17.65 a       | 28.44 a        | 24.73 a         | 30.16 b         | 26.32 a         | 45.16 c         |
| Melancholic     | 60.53 c        | 44.83 b        | 42.55 b         | 28.89 c         | 29.76 c         | 45.00 c         |

Note: Means with different superscripts are significantly different
6.3 Study II

6.3.1 Analyses of the relationship between depression and BMI

In order to test the hypothesis that measures of depression which include somatic symptoms will more strongly predict the relationship between BMI and depression, regression analyses predicting zBMI were conducted with CDRS-R, which assesses somatic symptoms, and RADS, which does not assess somatic symptoms.

In order to assess the importance of CDRS-R score as a predictor of BMI, a simple regression analysis with CDRS-R predicting zBMI was conducted. This model did not significantly predict zBMI ($\beta = 0.06$, $F = 1.52$, $p = 0.21$). In order to test the hypothesis that
the relationship between depression and BMI is stronger among females, regression analysis was conducted first with CDRS-R ($\beta = 0.04$) and sex ($\beta = 0.09$) ($F = 2.53$, $p = 0.08$) and then CDRS-R ($\beta = -0.21$), sex ($\beta = -0.20$) and their interaction ($\beta = 0.42$) predicting zBMI. The later overall model approached significance ($F = 2.57$, $p = 0.053$), but none of the predictors independently predicted zBMI (See table 7). When the same analyses were conducted using RADS total score to predict zBMI the model did not significantly predict zBMI ($\beta = 0.05$, $F = 1.36$, $p = 0.24$). When regression analyses were conducted first using RADS score ($\beta = 0.03$) and sex ($\beta = 0.09$) ($F = 2.31$, $p < .10$) and then RADS ($\beta = 0.15$), sex ($\beta = 0.32$) and their interaction ($\beta = 0.31$) as predictors, the model was not significant ($F = 1.79$, $p = 0.15$). Overall, these results are not consistent with the hypothesis that measures containing somatic symptoms would better predict zBMI among adolescents. In addition, although the addition of gender and the interaction of gender and CDRS-R improved model fit, neither model achieved significance, failing to provide support for the hypothesis that the predictive power of depression score (CDRS-R and RADS) for zBMI would be stronger among females.
Table 7
Regression Models of Depression Score Predicting Adolescent zBMI

<table>
<thead>
<tr>
<th>Predictor Variable</th>
<th>F</th>
<th>β</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main Effects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>2.53</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>CDRS-R</td>
<td>0.04</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.09</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>2.31</td>
<td>0.10</td>
<td></td>
</tr>
<tr>
<td>RADS</td>
<td>0.03</td>
<td>0.31</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.09</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td><strong>Interaction Effects</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>2.57</td>
<td>0.53</td>
<td></td>
</tr>
<tr>
<td>CDRS-R</td>
<td>-0.21</td>
<td>0.19</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>-0.2</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>CDRS-R*Sex</td>
<td>0.42</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td>1.79</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td>RADS</td>
<td>0.15</td>
<td>0.31</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>0.32</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>RADS *Sex</td>
<td>-0.30</td>
<td>0.37</td>
<td></td>
</tr>
</tbody>
</table>

Note: CDRS-R = Children’s Depression Rating Scale Revised, RADS = Reynold’s Adolescent Depression Scale

6.3.2 Depression Class as a Covariate

As part of the latent class analysis, each participant was assigned a membership likelihood for each class. Individuals with a likelihood greater than 0.6 were identified as class members. Individuals with a likelihood less than 0.4 were identified as not class members. Nineteen individuals with membership likelihoods between 0.4 and 0.6 could not be clearly assigned to either class as they were nearly equally as likely to be members of 2 classes and were therefore not included in multivariate analyses of the
relationship between weight and depression class. Thus, each participant included in these analyses was identified as a member of only one class.

Non-parametric Spearman correlation coefficients were conducted to identify latent classes associated with BMI percentile. Type I error was controlled for using the Holm-Bonferroni correction. Membership in classes 4 (r=.13, p<.005) and 6 (r=.14, p<.005), the hyperphagic classes, were associated greater numbers of participants with BMI percentile ≥95th. This is consistent with the hypothesis that hyperphagia associated with depression is related to obesity. Classes 3 and 5, the hypophagic classes were not significantly associated with BMI percentile ≥95th. This is not consistent with the hypothesis that hypophagia associated with depression is related to decreased weight.

![Figure 8 zBMI by Latent Class](image)

** Atypical Class was significantly different from Mild (p=0.001), Moderate (p=0.002), Mod w/ hyperphagia (p=0.004) and Melancholic (p=0.001)
ANOVA analysis of depression class predicting zBMI was significant ($\beta = 0.16$, $F=11.89$, $p=0.0006$). Table 8 compares the contributions of RADS, CDRS-R and depression class in separate models predicting zBMI. The table illustrates that depression class was the strongest predictor of zBMI ($\beta = 0.16$) and the model with depression class predicting zBMI was the only model that achieved significance ($F = 11.89$, $p=0.0006$). In addition, when sex and the interaction between depression class and sex were added to the model, depression class was the only significant contributor ($F = 3.54$, $p=0.0008$) to the significant model ($F=2.99$, $p=0.004$). When the contribution of individual classes was examined, only the Atypical class contributed significantly to the model, with membership in class 6 predicting elevated zBMI. (See table 9)

Table 8
Comparison of Regression Models of Depression Measures Predicting Adolescent zBMI

<table>
<thead>
<tr>
<th></th>
<th>$F$</th>
<th>$\beta$</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children's Depression Rating Scale Revised</td>
<td>1.52</td>
<td>0.06</td>
<td>0.21</td>
</tr>
<tr>
<td>Reynold's Adolescent Depression Rating Scale</td>
<td>1.36</td>
<td>0.05</td>
<td>0.24</td>
</tr>
<tr>
<td>Depression Class</td>
<td>11.89</td>
<td>0.16</td>
<td>0.0006</td>
</tr>
</tbody>
</table>
Table 9  
**Regression Model of Depression Classes Predicting Adolescent zBMI**

<table>
<thead>
<tr>
<th>Predictors of BMI</th>
<th>Parameter Estimate</th>
<th>Standard Error</th>
<th>P Value</th>
</tr>
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<tbody>
<tr>
<td>Intercept</td>
<td>0.59</td>
<td>0.17</td>
<td>0.0006</td>
</tr>
<tr>
<td>Sex</td>
<td>0.07</td>
<td></td>
<td>0.07</td>
</tr>
<tr>
<td>Males</td>
<td>-0.2</td>
<td>0.26</td>
<td>0.45</td>
</tr>
<tr>
<td>Depression Class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.17</td>
<td>0.22</td>
<td>0.42</td>
</tr>
<tr>
<td>Moderate with Hypophagia</td>
<td>0.2</td>
<td>0.23</td>
<td>0.34</td>
</tr>
<tr>
<td>Moderate with hyperphagia</td>
<td>0.36</td>
<td>0.32</td>
<td>0.12</td>
</tr>
<tr>
<td>Melancholic</td>
<td>0.06</td>
<td>0.31</td>
<td>0.83</td>
</tr>
<tr>
<td>Atypical</td>
<td>0.64</td>
<td>0.37</td>
<td>0.002</td>
</tr>
<tr>
<td>Depression Class*Sex</td>
<td>0.0029</td>
<td>0.07</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Note: Overall model - f=2.99, p=0.004

In order test the hypothesis that the inclusion of depression class in analyses examining the relationship between weight and depression improves model fit, depression class was added to the model for RADS. The model containing depression class, as well as RADS, sex, and their interaction showed notably improved fit (F=4.6, p<0.0012 compared to F=1.79, p=0.15 without depression class). In this model, depression class was the only significant predictor (F=3.49, p=0.004). This is consistent with the hypothesis that the inclusion of depression class in models of depression predicting BMI improves overall model fit. When the interaction of RADS score (as a measure of depression severity) and depression class was added to the model containing depression class, RADS score, sex and the interaction of sex and RADS score, overall fit of the model did not improve, suggesting that the contribution of depression class does not interact with severity of mood symptoms.
7. Discussion

This research sought to identify unique classes of depression with differential somatic symptom profiles that are associated with weight in order to clarify the relationship between depression and weight in adolescents. To date the research on the association between weight and depression has been inconsistent, although trends in the literature suggest that gender (Carpenter et al., 2000; Istvan et al., 1992) and age of depression onset (Richardson et al., 2003; R. E. Roberts et al., 2003) may be useful covariates when examining this relationship. However, depression subtype, characterized by unidirectional somatic symptoms, has not yet been considered as a covariate. This is particularly important, as these somatic symptoms are most likely to contribute to weight change. As these unidirectional somatic symptoms appear to be unique identifiers of MD and AD symptom profiles (Asnis et al., 1995; Khan et al., 2006), identification of AD and MD may be of critical importance when examining the relationship between depression and weight. Both the consistency of associations between depression and future weight change between adolescence and young adulthood in the literature (Franko et al., 2005; Kandel & Davies, 1986; Pine et al., 1997) and the increased prevalence of symptoms associated with weight gain among adolescents (Posternak & Zimmerman, 2002) suggest that adolescence may be a critical intervention point for both depression and obesity. Therefore, an adolescent population was selected in order to best inform future research examining interventions at this important developmental stage.
7.1 Study I

7.1.1 Latent classes of depression

Latent class analysis of participant responses on the CDRS-R revealed six classes of depression. Classes were both phenotypic and dimensional in character. In regard to the dimensional qualities of the identified latent classes, three dimensions were identified: mild, moderate and severe (Class 5 and 6). Consistent with the literature, the Melancholic class was associated with greatest severity (Khan et al., 2006) and the Atypical class showed significantly greater severity compared to all classes but the Melancholic class. This is consistent with the work of Benazzi (Benazzi, 2002b), who found that MD was associated with greatest symptom severity and AD was associated with somewhat less severity in comparison. Classes 2, 3, and 4 were not significantly different on either measure of symptom severity and therefore were identified as Moderate Depression, whereas class 1 showed low symptom probabilities and therefore was termed Mild Depression.

Unique phenotypic classes were also identified, based partly on differences in somatic symptoms, particularly phagic and to a lesser extent activity symptoms (ex. hypoactivity and listless speech in Class 6). The symptom profiles of classes 3 and 5 were both characterized by hypophagia. Class 5 most strongly resembles an MD profile. In addition to decreased appetite, Class 5 also loaded mostly strongly on depressed feelings, consistent with the marked depression symptoms described in the DSM-IV-TR. Also consistent with MD symptoms, Class 5 had the strongest loadings for terminal and
intermediate insomnia, as well as morbid and suicidal ideation. While these may simply reflect the elevated severity of symptoms associated with this class (these symptoms were only present in individuals with greatest severity of symptoms), they serve to support the identification of this class as Melancholic Depression in adolescents. In contrast, Class 3 was not uniquely associated with any symptoms other than increased appetite and showed greater association with class 2, Moderate Depression. This may be because symptoms associated with Melancholic Depression are rare among those with moderate severity, but even so, there is no evidence strong enough to consider class 3 a milder version of Melancholic Depression.

Classes 4 and 6 were associated with a 100% prevalence of hyperphagia. Similar to class 3, the profile of class 4 lacked additional characteristics associated with AD and showed greater association with class 2, Moderate Depression. In contrast, class 6, was associated with listless speech, flattened affect and hypoactivity, which are all consistent with AD. Note that these additional symptoms are suggestive of less energy expenditure, which is consistent with the hypothesis that AD symptoms are likely to contribute to a positive energy balance resulting in elevated BMI during a depressive episode.

The symptom profiles of classes 3 and 4 did not parallel the profile of the Melancholic and Atypical classes respectively. They were more closely associated with class 2, Moderate Depression and therefore should be considered taxometrically distinct from the AD and MD classes. This indicates that although phagic symptoms are clearly
one unique identifier among depressive classes, Atypical and Melancholic Depression are not the only classes that may be associated with weight change as previously hypothesized.

7.1.2 Correlates of Depression Class.

In regards to psychosocial correlates of the identified latent classes, consistent with its mild moniker, Class 1 was associated with lower scores on measures of comorbidity, and was not associated with any additional psychosocial variables. Class 2 was not significantly associated with any psychosocial variables after controlling for multiple comparisons. Both hyperphagic classes were associated with female gender. In regards to class 6, this is consistent with the literature on AD (Thase, 2007). However, class 6 was not associated with race, age, or greater comorbidity as has been previously found in examination of adult AD (Angst et al., 2002; Benazzi, 1999; J. W. Stewart et al., 2002; J. W. Stewart et al., 2005; M. E. Thase, 1997).

Further supporting the differentiation between the hypophagic classes, Classes 3 and 5 were disparate in their associations. Class 3 was associated with male gender, while class 5 was associated with female gender. While class 3 was associated with less comorbidity compared with the rest of the sample, class 5 was associated with more. In fact, class 5 was associated with comorbidity on nearly all measures and subscales.

7.1.3 Limitations

It should be noted that due to limitations of the data, LCA using all symptoms associated with AD and MD was not possible. Although different types of insomnia
were found to be differentially associated with depression, the absence of a measure of hypersomnia leaves the utility of sleep patterns in distinguishing depression subtypes unresolved. In addition, although the three forms of insomnia were not related to BMI, the inability to assess the full range of sleep disturbance likely limited effect size. Therefore, further examination of the role of sleep changes, including hypersomnia, in the identification of depression subtypes and their association with BMI is warranted.

Similarly, the full range of motoric differences, including psychomotor agitation, was not fully assessed and therefore its role in distinguishing classes cannot be determined. Although, consistent with the literature, LCA did reveal greater prevalence of hypoactivity in the Atypical class, the role of psychomotor agitation in Melancholic Depression could not be examined. It is possible that class 5 would have significant loadings on an item assessing agitation in addition to the weak loadings already noted for hypoactivity, which would support identifying these classes as adolescent MD.

7.1.3 Study I Conclusions

Results from latent class analysis indicated the presence of six latent classes for depression in adolescents. Four of these classes were associated exclusively with a unidirectional phagic symptom and two of those classes had profiles that were consistent with either MD or AD. These data not only support the existence of the AD and MD classes among adolescents, they also support the hypothesis that phagic symptoms are of particular importance when identifying depression subclasses.
7.2 Study II

This study hypothesized that the cause of inconsistent findings in the literature on weight and depression is a failure to distinguish between AD and MD, as the somatic symptom profiles of these depressive subtypes are likely to contribute to positive or negative energy balance. Previous research has identified phagic symptoms as key unique identifiers in these depressive subtypes (Benazzi, 2002a; Rush & Weissenburger, 1994). The clear role for unique phagic symptoms in the depression classes identified using LCA in this study is consistent with this literature. The uniqueness and consistency of phagic symptoms within classes that were consistent with AD and MD is consistent with the hypothesis that controlling for depression subtypes may clarify the relationship between weight and depression.

7.2.1 Association of depression score and BMI

In models predicting BMI from self-reported depression, neither the CDRS-R nor RADS predicted adolescent zBMI, with or without the addition of sex as a covariate. It was hypothesized that measures of depression which included somatic symptoms (CDRS-R) would better predicted zBMI compared to measures that do not assess somatic symptoms (RADS). Although a trend consistent with this hypothesis was noted, neither model was significant and therefore the null hypothesis cannot be rejected. Despite the failure of the measure with a greater somatic component to show a relationship with BMI, this is not to say that the identification of somatic symptoms is not useful in examining the relationship between weight and depression. Rather a
measure that assesses, but gives equal weight to, bidirectional somatic symptoms is not more predictive of weight due to the very nullifying effect hypothesized to be related to the inconsistencies in the literature on this topic.

Although the inclusion of sex and its interaction with depression score improved model fit, these models also failed to reach significance. Again, although a trend consistent with this hypothesis was noted, the null hypothesis cannot be rejected. This hypothesis was founded on literature that indicated greater prevalence of AD and hyperphagia among females (Matza et al., 2003). Despite failure to reach significance, hyperphagia was more common among girls (33%) than boys (20%) in this sample. Additionally, the Atypical and Moderate with Hyperphagia Classes were associated with female gender, which is consistent with the literature upon which the hypothesis was based. It is unclear why more hyperphagia in females did not result in a stronger relationship between BMI and depression among women. However, the expected pattern of a stronger association among females was present in the non-significant CDRS-R models, with notably better fit for predictive models of BMI in females compared to males.

### 7.2.2 Associations Between Depression Classes and BMI

Analyses were also conducted to examine the association of BMI with each of the classes. Only the hyperphagic and not the hypophagic classes in this sample were associated with BMI. The hypophagic classes were not associated with lower BMI as had been predicted. Thus, the original hypothesis that classes associated with hyperphagia
would be associated with elevated BMI and those with hypophagia would be associated with lower BMI was only partly confirmed. However, although not significant, the Melancholic class had the lowest BMI among the classes. It is possible that this relationship did not reach significance because other symptoms associated with the MD profile, such as fatigue, might counteract the decreased energy intake. It is also possible that individuals in this class are eating less volume or less frequently, but are consuming food of high caloric value, which would also decrease the effect of decreased appetite on weight. Finally, the lack of association between hypophagic classes and BMI may be related to the comparative ease of weight gain compared to weight loss (i.e. a caloric floor but no caloric ceiling effect in addition to changes in metabolism associated with weight loss).

7.2.3 Models with depression score and class

Although the inclusion of depression class in the RADS models improved model fit, the inclusion of the interaction term for depression class and RADS score did not significantly contribute to the overall fit the model. This suggests that the symptom profile, particularly profiles characterized by hyperphagia, contributes to differences in BMI among depressed adolescents independent of severity of depression. This supports the hypothesis that depression type is a useful independent predictor of BMI in depressed adolescents.
7.2.4 Limitations

It is unfortunate that the measures of depression used in this study did not enable the examination of the complete range of sleep and activity related depression symptoms with BMI. Therefore, it cannot be determined based on this data if the association noted between depression class and BMI are due to the combined effects of somatic symptoms within the class or only to phagic symptoms. Associations tested at the individual symptom level for hypoactivity, hypophagia and insomnia were not significant, whereas the association with hyperphagia was. It should be noted that the endorsement rate for the different types of insomnia was either very high in the case of initial insomnia or very low. In addition, endorsement of hypoactivity was typically at the mild-moderate level, with only 10%) endorsing dramatic decreases in activity. This contrasts phagic symptoms, which were present in every class member. Therefore, the effect of non-phagic somatic symptoms may be dwarfed by the prevalence of phagic symptoms. Analyses may not have had enough power to examine symptoms likely to have smaller effect sizes in comparison to that of phagic symptoms. It is notable that endorsement levels of these symptoms were broadly consistent with AD and MD profiles and therefore a significant role for these non-phagic somatic symptoms when combined together cannot be ruled out, particularly as hypersomnia and leaden paralysis were not directly assessed.

Finally, we do not have pre-depression BMI for these participants. It is possible that participants in the hypophagic classes were overweight prior to their depressive
episode and despite losing weight since their depression onset have not lost enough to fall on the lower end of BMI in this sample. It is also possible that this is the case for the hyperphagic classes (i.e. class members had greater BMI prior to depression onset), which would eliminate depression as a possible cause of their elevated BMI status. Further study and replication of these results using longitudinal data will be necessary to clarify this association.

### 7.2.5 Study II Conclusions

In conclusion, these findings suggest that adolescents with symptom profiles characterized by hyperphagia are at risk for elevated BMI even after a relatively short duration. These results also highlight the importance of depression subtype in determining risk for obesity among depressed adolescents and suggest that only identifying AD and MD may not be sufficient to fully control for the effect of somatic symptoms, as the Moderate Hyperphagic class was also associated with BMI. As no previous research on weight and depression in adults or youth has included depression subtype in their analyses, these findings support the hypothesis that previous inconsistent results may be explained by this oversight.

### 7.3 Possible Mechanisms

There are several mechanisms by which depression may influence weight and vice versa. The complex neuroendocrine associations shared by appetite, metabolism and depression suggest a biological basis for any relationship between weight and depression. Eating behavior and mood states are both regulated, in part, by the
serotonergic system (Li et al., 2005; Masand, 2000; Weigle, 2003). Van Praag and Korf (1971). Several studies indicate that approximately 40% of depressed patients have a deficit in central serotonin metabolism, based on evidence that the serotonin metabolite 5-HIAA is abnormally low in the lumbar cerebrospinal fluid of depressed patients (Ashberg, Traskman, & Thoren, 1976; Post & Goodwin, 1978; Van Praag, Korf, & Schut, 1973). Research has indicated that increased carbohydrate consumption may contribute to increased serotonin synthesis, which may result in improved mood, particularly for obese individuals (Fernstrom & Wurtman, 1971; Lieberman, Wurtman, & Chew, 1986; Lyons & Truswell, 1988; Wurtman et al., 1985; Wurtman, 1993; Wurtman & Wurtman, 1996), however recent research has cast doubt on this hypothesis (Fernstrom & Fernstrom, 1995; Teff, Young, & Blundell, 1989; Teff, Young, Marchand, & Botez, 1989).

There is considerable evidence that leptin functioning is altered in individuals with depression (Antonijevic et al., 1998; Deushel et al., 1996; Esel et al., 2005; Gecici et al., 2005; Lu, 2007; Lu, Kim, Frazer, & Zhang, 2006; Pasco et al., 2008; Westling, Ahrin, Trdskman-Bendz, & Westrin, 2004). However, the results in the leptin and depression literature are nearly as inconsistent as the depression and obesity literature with depressed individuals showing no difference in leptin (Deuschle, 1996), increased leptin (Antonijevic et al., 1998; Gecici et al., 2005; Pasco et al., 2008) and lower leptin (Kraus, Haack, Schuld, Hinze-Selch, & Pollmdcher, 2001; Westling et al., 2004) compared to controls. Similar to the depression literature, gender effects have been noted (Esel et al., 2005; Pasco et al., 2008). However, in the case of leptin, elevated levels, which should
decrease appetite, have been found in women. In addition, a study examining leptin levels in individuals with AD showed elevated leptin levels (Gecici et al., 2005). This is inconsistent with increased prevalence of hyperphagia among women and individuals with AD. Leptin resistance may play a role in this relationship, with decreased leptin sensitivity resulting in increased appetite despite adequate leptin levels. Overall, these inconsistent findings strongly suggest that a heretofore unidentified moderator, possibly depression subtype, explains these inconsistent findings.

7.3 Implications

First and foremost, this research has significant implications for future research examining weight and depression. These results suggest that assessment for depression subtype and inclusion of subtype as a co-variate in analyses of weight and depression will improve predictive models and result in greater consistency in the literature. In addition, the inclusion of depression subtype in research examining relationships of obesity associated health conditions such as type 2 diabetes and hypertension, may improve power, clarify relationships and ultimately lead to more targeted interventions based on depression subtype in these populations.

This research also has implications for our understanding of the pathophysiology of depression, particularly in the neuroendocrine system. Research has already demonstrated differential functioning of the HPA axis in individuals with MD and AD, with AD patients showing CRH deficiency and MD patients demonstrating increased CRH activation (Gold & Chrousos, 2002). Serotonergic functioning, which has
been closely linked to appetite and weight regulation may differ between depression
groups as well. Fourteen different serotonin receptors exist. Differences in appetitive
symptoms among individuals with MD and AD may be related to dysfunction in
different serotonin receptors. For example, recent research has identified the serotonin
receptor 5-HT\textsubscript{2c} as potentially important in body weight maintenance (Nonogaki, Strack,
Dallman, Teott, 1998) and the drugs sibutramine and fenfluramine, both SSRIs used for
weight loss, target the 5-HT\textsubscript{2c} receptor (see Vickers & Dourish, 2004 for a review). Future
research may discover that dysfunction of the 5-HT\textsubscript{2c} receptor may be associated with
AD rather than MD. Similar to the literature on weight and depression, previous
research examining the relationship between depression treatment with SSRIs and
weight outcomes have been inconsistent with some studies showing weight loss (Stock,
1999, James, et al. 2000, Wirz-Justice, Van der Velde, Bucher, Nil, 1992, Gadde, Parker,
Maner, Wagner, Logue, Drezner, Krishnan, 2001, Li et al. 2005, (Darga, Carroll-Michals,
Botsford, Lucas, 1991, Vanina, Podolskaya, Sedky, Shahab, Siddiqui, Munshi, Lippmann,
2002), gain (Sussman, Ginsberg, & Bikoff, 2001) or no change at all (National Task Force
on the Prevention and Treatment of Obesity, 1996; Masand, 2000) possibly depending on
which SSRI is prescribed (Fava, Judge, Hoog, Nilsson, Koke, 2000). The inclusion of
depression subtype in these studies may help clarify these results, leading to better
informed prescription decisions dependent on subtype of depression and their expected
weight related side effects.
Consistent with previous research, this study indicates that symptom profiles that are broadly consistent with DSM criteria for AD and MD exist among adolescents. It also suggests that somatic symptoms may be the most useful unique identifiers for these two subtypes. As such, symptoms such as interpersonal sensitivity and extreme anhedonia may not be useful in identifying depression subtype among adolescents, as parallel symptoms such as social withdrawal and low self-esteem were present in all but the least symptomatic classes. The latent class profile consistent with MD exhibited the highest level of severity and greatest number of comorbidities. This class was equally as common as other classes in this sample, suggesting that when using MD criteria are empirically modified for adolescents, MD is not notably less prevalent in this population as has been previously suggested. Although it is unclear if these MD and AD classes parallel their adult counterparts in their treatment response profiles, the identification of unique classes of depression among adolescents may inform the development and application of assessment strategies and treatments that might be tailored to these common symptom patterns. Finally, better understanding of depression subtypes among adolescents will likely serve to better characterize individual cases of depression, aid in the identification of comorbidities, inform treatment and better project illness course.

Should future research replicate this association between depression subtype and weight, several clinical implications apply. First, clinicians who diagnose adolescents with AD should be aware of the potential for weight gain and should be prepared to aid
patients in efforts to maintain their weight or to lose extra pounds. These individuals may gain particular benefit from regular exercise, which would both serve to improve mood and to counteract weight gain related to AD. As previously mentioned, it is also possible that these individuals would be more likely to respond to certain antidepressant drugs with improvement in both depression and weight. Previous research with adults has shown better response to tricyclic medications in individuals diagnosed with MD and better response to MAOIs in individuals with AD. Thus, knowledge of type of depression could potentially guide pharmacotherapy and psychotherapy (J. W. Stewart, 2007) to more individualized and effective treatments.

Adolescence is often the point of origin for the development of AD and as such represents a potentially powerful point of intervention in this serious and recurrent illness. Not only would successful intervention improve psychosocial outcomes, it may also improve health outcomes by averting weight gain associated with AD symptoms.

7.4 Overall Limitations and Future Directions

These results should be interpreted in the context of six potential methodological limitations that may be addressed in future research.

Interpretation of the findings of this study are limited by the cross sectional nature of the data. Therefore, any causal relationship between weight and depression cannot be inferred. Future analysis of the relationship between weight and depression should utilize longitudinal designs in order to identify any causal relationships.
The current study is largely based on adolescent responses on a single measure at a single time-point, the CDRS-R. Analysis of parent and clinician report data may provide corroborating evidence as to the validity of the identified depression classes. In addition, repeated measures research would assess the stability of these classes over time within the same population, further validating the class structure.

As previously mentioned, the adolescent self-report measure used in these analyses did not assess for all symptoms of depression identified in the DSM-IV. In particular, hypersomnia, psychomotor agitation and leaden paralysis were not specifically assessed. Although the current analysis resulted in classes consistent with AD and MD, a measure that includes these missing symptoms is needed to obtain complete profiles of depression classes and compare those classes to DSM-IV defined MD and AD. The results of this latent class analysis should be replicated using measures that fully assess symptoms of DSM subtypes, including hypersomnia, psychomotor agitation, leaden paralysis, interpersonal sensitivity, and diurnal patterns of symptom severity. Inclusion of these items will be key in confirming or disproving the importance of somatic symptoms within these classes. It is also possible that the inclusion of these symptoms will help clarify more ambiguous class profiles.

Although this sample was obtained through public advertisement in multiple cities and not solely from inpatient or outpatient clinic populations, this is still a treatment seeking sample (Shapiro et al., 1984). As only a small proportion of individuals affected with major depression are in specialist care, other classes of
depression with characteristics associated with individuals who do not seek treatment might emerge through epidemiologic designs. In addition, epidemiologic designs do not exclude individuals with subthreshold symptoms. Therefore, a more complete typology of depressive classes may emerge from epidemiologic samples.

The responses on the CDRS-R are imposed on a 7-point scale. However, latent class analysis requires dichotomous variables. Responses were therefore coded as present/not present with the somewhat stringent requirement that responses of 1-3 were coded as not present, whereas responses greater than 3 were coded as present. As a consequence, some of the richness of this data was lost in favor of classes based on symptom profile (i.e. which symptoms are most likely to occur in a class) rather than a profile that indicates the likely severity of individual symptoms within each class.

Finally, while LCA can indicate when a pattern of observed symptoms in a population is consistent with the existence of discrete latent classes, it cannot prove that such discrete classes exist. It is possible that the classes of depression observed in this sample reflect only differing points on a single underlying continuum of severity.
## Appendices

### Table 10

*Additional Adolescent Psychological Characteristics by Gender*

<table>
<thead>
<tr>
<th></th>
<th>Total N = 496</th>
<th>Males n = 231</th>
<th>Females n = 265</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td><strong>CASS</strong></td>
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<tr>
<td>Family Problems</td>
<td>59.37</td>
<td>10.62</td>
<td>59.24</td>
</tr>
<tr>
<td>Emotional Problems *</td>
<td>60.86</td>
<td>10.31</td>
<td>59.56</td>
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<tr>
<td>Conduct Problems **</td>
<td>56.77</td>
<td>11.24</td>
<td>54.82</td>
</tr>
<tr>
<td>Cognitive Problems ***</td>
<td>60.96</td>
<td>11.23</td>
<td>58.27</td>
</tr>
<tr>
<td>Anger Problems</td>
<td>57.94</td>
<td>10.70</td>
<td>57.30</td>
</tr>
<tr>
<td>Hyperactivity **</td>
<td>52.75</td>
<td>10.90</td>
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</tr>
<tr>
<td>ADHD *</td>
<td>62.61</td>
<td>11.43</td>
<td>61.14</td>
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Figure 9 Comparison of Profiles of Moderate with Hypophagia and Atypical Classes
Figure 10 Comparison of Profiles of Moderate w/ Hyperphagia and Melancholic Classes
Table 11

Mean Psychosocial Scores by Depression Class

<table>
<thead>
<tr>
<th></th>
<th>1</th>
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<th>4</th>
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<tbody>
<tr>
<td>CGIS***</td>
<td>57.84±10.33</td>
<td>56.80±9.89</td>
<td>56.59±10.90</td>
<td>57.37±12.19</td>
<td>55.21±11.13</td>
<td>56.53±10.82</td>
</tr>
<tr>
<td>CDRS***</td>
<td>29.39±5.98</td>
<td>52.34±10.43</td>
<td>50.78±9.16</td>
<td>53.85±9.16</td>
<td>66.13±9.71</td>
<td>58.37±12.92</td>
</tr>
<tr>
<td>RADS***</td>
<td>64.89±14.40</td>
<td>76.80±13.31</td>
<td>75.87±13.97</td>
<td>80.48±13.97</td>
<td>89.02±10.43</td>
<td>79.35±12.76</td>
</tr>
<tr>
<td>BHS (NS)***</td>
<td>6.29±5.03</td>
<td>9.99±5.70</td>
<td>8.82±5.14</td>
<td>9.93±5.71</td>
<td>12±5.31</td>
<td>9.77±5.50</td>
</tr>
<tr>
<td>SIQ***</td>
<td>11.82±17.16</td>
<td>21.54±19.73</td>
<td>16.40±19.53</td>
<td>25.57±20.08</td>
<td>36.16±23.76</td>
<td>25.41±24.29</td>
</tr>
<tr>
<td>PQ-LES-Q***</td>
<td>51.00±7.89</td>
<td>44.08±7.77</td>
<td>44.84±8.89</td>
<td>41.70±8.15</td>
<td>38.58±8.44</td>
<td>43.17±9.12</td>
</tr>
<tr>
<td>MASC Total***</td>
<td>40.54±15.59</td>
<td>48.99±17.26</td>
<td>45.47±18.27</td>
<td>49.30±15.09</td>
<td>56.14±17.00</td>
<td>50.25±17.31</td>
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<tr>
<td>Perfectionism (NS)</td>
<td>46.34±10.46</td>
<td>47.29±9.91</td>
<td>45.93±10.78</td>
<td>45.63±10.51</td>
<td>47.00±11.27</td>
<td>57.17±10.50</td>
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<tr>
<td>Somatization***</td>
<td>46.92±9.38</td>
<td>52.66±10.51</td>
<td>51.72±11.31</td>
<td>52.63±9.26</td>
<td>57.43±10.54</td>
<td>53.22±10.11</td>
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<td>Physical Symptom**</td>
<td>49.16±9.77</td>
<td>55.52±10.84</td>
<td>54.34±11.00</td>
<td>55.15±9.43</td>
<td>60.82±9.69</td>
<td>57.17±10.50</td>
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<tr>
<td>Separation / Panic*</td>
<td>51.86±11.14</td>
<td>51.33±11.56</td>
<td>51.19±11.91</td>
<td>52.24±11.47</td>
<td>54.47±12.03</td>
<td>54.93±12.34</td>
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<td>Humiliation / Rejection*</td>
<td>54.03±10.78</td>
<td>59.48±12.68</td>
<td>57.35±13.20</td>
<td>59.52±12.86</td>
<td>61.80±12.46</td>
<td>57.22±11.94</td>
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<td>Social Anxiety (NS)</td>
<td>55.65±11.14</td>
<td>60.64±12.79</td>
<td>58.04±13.22</td>
<td>59.24±13.32</td>
<td>62.13±12.83</td>
<td>57.30±11.83</td>
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Table 11 Continued

CASS

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<th>58.16±10.57&lt;sup&gt;c&lt;/sup&gt;</th>
<th>59.16±10.12</th>
<th>57.33±10.34&lt;sup&gt;f&lt;/sup&gt;</th>
<th>62.20±10.74&lt;sup&gt;abde&lt;/sup&gt;</th>
<th>61.07±11.39&lt;sup&gt;a&lt;/sup&gt;</th>
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<td>Family Problems*</td>
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<td>58.42±10.34&lt;sup&gt;e&lt;/sup&gt;</td>
<td>61.54±8.41&lt;sup&gt;ae&lt;/sup&gt;</td>
<td>66.87±7.97&lt;sup&gt;abcdef&lt;/sup&gt;</td>
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<td>Emotional Problems***</td>
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<td>56.77±11.57</td>
<td>54.87±10.04&lt;sup&gt;e&lt;/sup&gt;</td>
<td>56.43±12.62</td>
<td>59.39±11.35&lt;sup&gt;ac&lt;/sup&gt;</td>
<td>57.62±12.43</td>
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<td>59.45±10.45&lt;sup&gt;e&lt;/sup&gt;</td>
<td>63.09±12.49&lt;sup&gt;e&lt;/sup&gt;</td>
<td>65.23±11.14&lt;sup&gt;abcdef&lt;/sup&gt;</td>
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<td>Cognitive Problems**</td>
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<td>60.41±8.68&lt;sup&gt;bc&lt;/sup&gt;</td>
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<td>Hyperactivity**</td>
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<td>62.78±10.23&lt;sup&gt;e&lt;/sup&gt;</td>
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Note: CGIS = Child Global Impression Scale, CDRS-R = Children’s Depression Rating Scale Revised, RADS = Reynold’s Adolescent Depression Scale, BHS = Beck Hopelessness Scale, SIQ = Suicidal Ideation Questionnaire-Jr, PQ-LES-Q = Pediatric Quality of Life Enjoyment and Satisfaction Questionnaire, MASC = Multidimensional Anxiety Scale for Children, CASS = Conners’ Wells’ Adolescent Self-report Scale
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