

**Refractory Eating Disorders in Youth: An Examination of
Predictors, Profiles and Growth Trajectories**

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Table of Contents

Refractory Eating Disorders in Youth: An Examination of Predictors, Profiles and	
Growth Trajectories	1
Acknowledgements.....	2
Table of Contents	3
List of Tables	7
List of Figures	8
General Introduction	9
What is an Eating Disorder?	11
Refractory Eating Disorders	14
Theoretical Mechanisms of Refractory Eating Disorders.....	17
Objectives of Current Study.....	19
References.....	22
Study 1: Predictors of Refractory Eating Disorders in a Clinical Sample of	
Adolescents	33
Abstract.....	34
Introduction.....	35
Methods.....	41
Participants.....	41
Description of Eating disorder program	41
Assessment Measures	43
Procedures.....	45

Analytic Plan.....	46
Results.....	46
Discussion.....	49
References.....	56
Table 1	64
Table 2.	65
Study 2: Identifying Profiles of Refractory Cases in Adolescents with Eating Disorders:	
A Latent Profile Analysis.....	66
Abstract.....	67
Introduction.....	68
Methods.....	74
Participants.....	74
Description of Eating disorder program	75
Assessment Measures	76
Procedures.....	79
Analytic Plan.....	79
Results.....	82
Descriptive Statistics.....	82
Initial Intake Assessment Data.....	83
Residual Change Score Data.....	84
Comparison of classifications	86
Discussion.....	86
Limitations	91

Future Directions	91
References.....	94
Table 1.	103
Table 2.	104
Table 3.	105
Table 4.	106
Table 5.	107
Study 3: Growth Trajectories of Maintenance Variables Related to Refractory Eating Disorders in Youth.....	
Abstract.....	109
Growth Trajectories of Maintenance Variables Related to.....	110
Refractory Eating Disorders in Youth	110
Methods.....	116
Participants.....	116
Description of Eating disorder program	116
Assessment Measures	118
Procedures.....	119
Analytic Plan.....	119
Results.....	122
Descriptive Statistics.....	122
Confirmatory Factor Analysis of Summary Maintenance Variable	123
Growth Curve Trajectories	123
Refractory Status as a Predictor of Variability in Growth Curves.....	125

Discussion.....	125
Limitations	127
Future Directions	128
Conclusions.....	129
References.....	130
Table 1.	138
Table 2.	139
Table 3.	140
Figure 1.....	141
Figure 2.	142
General Conclusion.....	143
References.....	151

List of Tables

Study 1: Predictors of Refractory Eating Disorders in a Clinical Sample of Adolescents

Table 1. Means (SD) and reported ranges for all predictors separately for single-episode and refractory groups.....	34
Table 2. Sequential logistic regression of refractory status predicted by ED related refractory and maintenance variables	65

Study 2: Identifying Profiles of Refractory Cases in Adolescents with Eating Disorders:

A Latent Profile Analysis

Table 1. Descriptives of latent class indicators across full sample.....	103
Table 2. Results of Latent Profile Analysis of Intake Assessment data	104
Table 3. Means, standard errors, and ANOVA results for the latent class indicators for initial assessment data.....	105
Table 4. Results of Latent Profile Analysis with Residual Change Scores	106
Table 5. Means, standard errors, and ANOVA results for the latent class indicators for residual change scores across the first treatment encounter.....	107

Study 3: Growth Trajectories of Maintenance Variables Related to Refractory Eating

Disorders in Youth

Table 1. Means and standard deviations of indicator variables divided by timepoint	138
Table 2. Growth curve estimates for the summary maintenance factor	139
Table 3. Growth curve estimates for the summary maintenance factor with refractory status as a time-invariant predictor	140

List of Figures

Figure 1. Standardized estimates of the measurement model for the summary maintenance factor.....	141
Figure 2. Growth curve pattern of summary maintenance factor for full sample.....	142

Refractory Eating Disorders in Youth: An Examination of Predictors, Profiles and Growth Trajectories

Eating disorders (EDs) are known as a debilitating group of disorders that are especially prevalent in female adolescents and young women (Fairburn, Cooper, Doll, Norman, & O'Connor, 2000; Goni & Rodriguez, 2007; Lewinsohn, Striegel-Moore, & Seeley, 2000). What was once viewed as a disorder exclusively affecting Caucasian upper-middle class young women from Western countries is now spreading across all demographics, crosscutting genders, ethnicities, and developmental periods (French, Story, Remafedi, Resnick, & Blum, 1996; Neumark-Sztainer, Story, Falkner, Beuhring, & Resnick, 1999). Anorexia nervosa (AN) has been named as one of the greatest mental health concerns for young people, with strong evidence showing that adolescents are at greatest risk for the onset of this disorder often in relation to the commencement of puberty (Bryant-Waugh, 2006; Lock & Gowers, 2005). Some of this concern is due to AN being cited as the psychiatric illness with the highest mortality rate either due to medical complications or suicide (Reijonen, Pratt, Patel, & Greydanus, 2003).

Eating disorders rank as the third most common chronic illness among adolescent females (Fisher et al., 1995), and have been ranked by the World Health Organization as one of the priority mental illnesses for children and youth (World Health Organization, 2004). Equally troubling is that EDs have been described as being 'high-priced' both in terms of healthcare dollars and in mortality rates (Krauth, Buser, & Vogel, 2002; Simon, Schmidt, & Pilling, 2005; Striegel-Moore, Leslie, Petrill, Garvin, & Rosenheck, 2000)- a concern that persists well past adolescence. With reviews of long-term outcome studies finding a poor recovery rate of just 57% (Steinhausen, 2002), the need to understand

adolescent EDs and their outcomes is imperative, as this group of disorders is plagued with a debilitating and long mental and physical course of illness.

Eating disorders are known for their chronic and relapse-ridden course (Fairburn et al., 2000; Lewinsohn et al., 2000). The cyclical nature of these disorders poses not only grave physical and mental health risks for the sufferer (Goldstein et al., 2011), it also presents serious challenges for the treating professionals (Strober, 2004) and places a high demand and cost on the health care system (Richard, Bauer, & Kordy, 2005). In spite of extensive research, no reliable predictors of long-term EDs have been identified (Strober, 2004) in either adult or adolescent populations, nor have treatments emerged that are specifically targeted towards treating those with a long-term ED. With gross estimates suggesting that one out of three individuals will suffer from a lengthy course of the illness (Richard et al., 2005), the prognosis for those diagnosed with an ED is compromised. Thus, it is fundamental to understand who is at risk and what factors are involved in long-term EDs, as the clinical and treatment implications gleaned from this evidence could be quite impactful.

The current project will include three studies that will explore long-term EDs in a large transdiagnostic sample of adolescents with an ED. It will also attempt to overcome methodological limitations associated with past studies of this type (Salbach-Andrae et al., 2009), and apply an operational definition of this course of illness that may provide a more reliable and valid method with which to identify these cases. As such, the use of the term **refractory ED**, defined as a return to same-type treatment, will be applied to best identify this group. Reasons and theoretical underpinnings for use of this definition will be explained. Together these three studies will fill a significant gap in the literature on

refractory course of illness in pediatric eating disorders. These studies will provide long overdue information on predictors, profiles and growth trajectories of those adolescents who suffer from a refractory course of an ED.

What is an Eating Disorder?

There are three main categories of eating disorders found in the DSM-IV (American Psychiatric Association, 2000): AN, bulimia nervosa (BN), and eating disorders not otherwise specified (EDNOS). Both AN and BN share the characteristics of disturbance in weight or shape perception and undue influence of weight and shape on the evaluation of oneself (American Psychiatric Association, 2000). The two disorders differ in that AN is primarily identified by a refusal to maintain one's weight above 85% of an individual's ideal body weight for their age and gender, as well as the absence of at least three consecutive menstrual cycles (females only). Meanwhile, the primary characteristic of BN is recurrent binge eating followed by some method of compensation, which occurs at a frequency of at least twice weekly for three months. Prevalence rates of AN are estimated to occur in 0.2 to 3.7% of young females and adolescents (American Psychiatric Association, 2006; Lucas, Beard, O'Fallon, & Kurland, 1991) and in approximately 1% of males, while the prevalence rates of bulimia nervosa are reported at 1 to 2% in young females (Wilson, Becker, & Heffernan, 2003) and 0.5% in males (Hudson, Hiripi, Pope, & Kessler, 2007).

The third category of eating disorders, EDNOS, usually refers to those individuals who do not meet the stringent criteria for AN or BN (Kohn & Golden, 2001). Although no formal agreed upon prevalence rates are available for this subgroup, some evidence has suggested rates of 14.6% for females (Hudson et al., 2007), while a recent

international study demonstrated that EDNOS is the most common ED encountered by health care professionals in routine clinical practice (Fairburn & Bohn, 2005). Others have shown that EDNOS is an especially common diagnosis in adolescents (Commission on Adolescent Eating Disorders, 2005), and that it carries the same severity of illness equivalent to that of AN or BN (Fairburn & Bohn, 2005). This diagnostic category is also characterized as heterogeneous in terms of the presentation characteristics of those with EDNOS (Eddy, Doyle, Hoste, Herzog, & le Grange, 2008), thus increasing the difficulty of studying this subgroup as a whole. Due to the heterogeneity of EDNOS, very limited research has been conducted on this large diagnostic category in adults and youth.

Empirically tested and evidence-based treatments for youth with EDs are scarce. At the current time, only family-based treatment (FBT) based on Maudsley principles (Lock & le Grange, 2005; Lock & Fitzpatrick, 2007) has been studied and found to be effective in clinical samples of youth with AN (e.g. Lock, Agras, Bryson, & Kraemer, 2005). Cognitive-behavioural approaches for AN have also been applied and tested with some success (e.g. Garner, Vitousek, & Pike, 1997), although arguably, very limited evidence exists for adolescent populations. Treatment approaches for BN differ from those that have been postulated for AN patients. In adult studies, two common treatment modalities have been cognitive-behavioural (CBT) and interpersonal therapy (IPT). A manual-based CBT approach has been shown to be superior to other psychological treatments in the short-term (Wilson & Fairburn, 2002), and successes with a group-based approach have also been demonstrated (Chen, Touyz, Beumont, Fairburn, Griffiths, Butow, et al., 2003). Similarly, IPT has also been shown to have some favourable treatment effects for those with BN (Fairburn, Jones, Peveler, Hope, &

O'Connor, 1993). Although several treatment approaches for EDs are available, very limited evidence exists that demonstrates the effectiveness of these treatments at targeting the chronicity of the disorder.

Other characteristics of the EDs, is that outcome studies reveal a poor long-term prognosis. In the adult ED literature, published relapse rates vary from 30% (e.g. Olmsted, Kaplan, & Rockert, 2005) to 63% (Field et al., 1997). In a review of 119 studies of AN patients followed for 10 years or longer, only 57.1% made a full recovery, 25.9% reported residual symptoms, 16.9% remained severely ill and chronic, and 1.8% died of AN related causes (Steinhausen, 2002). The prognosis for those with BN presents with a similar picture, with estimates of 21% to 75% attaining remission (Ben-Tovim et al., 2001; Fichter & Quadflieg, 2004; Grilo et al., 2003; Herzog et al., 1999; Keel, Dorer, Franko, Jackson, & Herzog, 2005). In a review study of BN samples, 88 studies with a follow-up period ranging from 5 to 10 years revealed recovery rates of just over 50% (Keel & Mitchell, 1997).

What is notable when reviewing the evidence on long-term outcomes of EDs, is the wide range of relapse rates presented in the literature. The large discrepancies in relapse rates have been credited to several reasons. Some have attributed it to the different operational definitions for recovery, relapse, or remission (Quadflieg & Fichter, 2003; Steinhausen, 2002; Walsh, 2008), whereas others have attributed it to the varying follow-up periods studied spanning 12 months to 15 years (e.g. Salbach-Andrae et al., 2009; Strober, Freeman, & Morrell, 1997), the small sample sizes, and the diagnostic and sampling heterogeneity of the samples (Holle et al., 2008). Similarly, comparisons across different treatment techniques or orientations, as well as comparing treatments of

differing lengths and intensities, might also be contributing to these discrepancies. Much work is still needed to achieve a consensus on how best to identify and label those with a long-term ED.

Refractory Eating Disorders

There has been a significant historical progression in the operationalization of a long-term ED, mostly related to what defines recovery of this disorder. Originally, recovery was defined to include only medical or physical indices such as weight and menstrual status (as apparent from Morgan-Russell's original criteria; Morgan & Russell, 1975), then the addition of behavioral indices (i.e. abstinence from binge eating, restricting, purging) were included in the definition to represent the multidimensionality of the disorder (Bulik, Sullivan, Fear, & Pickering, 2000; Strober et al., 1997). Now, these definitions have progressed to include psychological measures such as body image concerns and fear of gaining weight (Bachner-Melman, Zohar, & Ebstein, 2006; Couturier & Lock, 2006). A recent study designed to define adolescent AN recovery has demonstrated that both weight and psychological symptoms seem to play equal roles in defining recovery (Couturier & Lock, 2006). It also found that physical recovery typically occurs prior to psychological recovery. In this study of 86 adolescents with AN, the researchers found that the mean time for physical recovery was 11.3 months, whereas the mean time for psychological recovery was 22.6 months. Further studies have also confirmed that recovery of physical symptoms almost always occurs prior to psychological recovery (e.g. Fichter, Quadflieg, & Hedlund, 2006; Strober et al., 1997). The lack of consistent indices of recovery that span the current literature further complicate our understanding and ability to predict this type of course of illness, and

have led to inconsistent recovery rates depending on whether behavioural, cognitive, and/or psychological indices were applied.

Differences in the length of follow-up periods used when studying long-term outcomes of EDs, have led to conflicting results. For example, a study that was focused on short-term outcomes of adolescent AN reported that 1 year following discharge from a specialized ED inpatient program based primarily on a cognitive behavioural approach, 28.1% of the cases were fully recovered, 8.8% had some residual symptoms, and 59.6% had poor outcomes (Salbach-Andrae et al., 2009). Comparing this to a recent large European collaborative project that tracked over 600 individuals with either AN or BN, who received psychotherapeutic and psychodynamic treatment in a hospital-based setting for 2.5 years (Richard et al., 2005) provides different results. This study reported relapse rates of 32.6% for AN and 37.4% for BN after 2.5 years. Yet in a longer-term large adult study, 11% with AN and 10% with BN were considered recovered at the 10 year follow-up, whereas recovery rates increased to 16% and 25% for AN and BN respectively after 15 years (Holle et al., 2008), although there is no mention of the type of treatment received. Taken together, these studies suggest a poor course of illness, with many relapsing even 15 years after disease onset. More importantly, the mixture of results from these studies differ due to the difference in length of follow-up periods that were investigated, therefore operational definitions of this course of illness should avoid needing to depend on a timeframe in order to classify individuals who have relapsed.

Other contributory factors to the mixed and sometimes contradictory evidence are the length of time that symptom abatement must occur for recovery to be considered and the lack of transdiagnostic studies. To date, there are no consistent guidelines as to how

much time qualifies as a period of recovery. Duration of symptom abatement has ranged from 8 weeks to 3 years (Bachner-Melman et al., 2006; Herzog et al., 1999; Holle et al., 2008; Kordy et al., 2002), likely contributing to the vast discrepancies in recovery rates. Furthermore, the majority of this literature has mostly concerned individuals with AN or BN. Only one study was found that examined a transdiagnostic adult sample of EDs (McFarlane, Olmsted, & Trottier, 2008). Even more troubling is that there is no research examining recovery rates or relapses in adolescents who present with a diagnosis of EDNOS, despite the fact that this ED category is the one most often diagnosed in the adolescent population (Commission on Adolescent Eating Disorders, 2005).

In reviewing the many terms and concepts that have been used throughout the literature to delineate poor long-term outcomes in the EDs, it becomes apparent that there is no clearly agreed upon nomenclature to describe this illness course. Recovery and remission remain somewhat subjective and have historically been poorly defined. The concept of relapse also has inconsistent definitions that vary according to the length of the follow-up period observed and the definition of recovery used. The term rehospitalization usually refers to only those with AN who typically require inpatient hospitalization, and does not lend to other treatment modalities or ED categories. This array of terms that share some overlap but also many subtle differences, highlights that fact that there is no consensus in the nomenclature and definition of this type of illness course.

In order to overcome many of the limitations described with regards to an operational definition of this subgroup of patients, the current project will use a concrete definition that does not depend on the current definitional issues related to recovery or

relapse. While the operational definition can be focused on who recovers, it is also possible to focus the operational definition on return to same-type treatment. Focusing on the latter allows us to accurately identify a subgroup that is refractory or treatment-resistant, regardless of how recovery is defined, as those who merit return to the same type of treatment have undoubtedly experienced a return of the ED. This method will provide a more reliable and valid method of identifying those with a refractory course, without needing to depend on operational criteria for recovery that have not yet been established or agreed upon by researchers and clinicians in this literature.

Theoretical Mechanisms of Refractory Eating Disorders

Only a few theories relating to refractory EDs have been proposed to date. Fairburn and colleagues' (Fairburn, Cooper, & Cooper, 1986) cognitive-behavioural model for bulimia nervosa is among the first eating pathology maintenance model that has been proposed and empirically tested (Byrne & Mclean, 2002; Fairburn et al., 2003). This model posits that eating, weight and shape over-concern and evaluation is the primary maintaining factor in binge eating. The model further contends that binge eating in turn leads to the use of extreme compensatory behaviours in pursuit of the thin ideal. In this fashion, dieting is conceptualized to act as a mediator between appearance over-evaluation and bulimic symptoms, providing a maintenance factor to the disordered eating.

The term maintenance factor is often cited in this literature as those factors thought to help maintain a disease state. Stice (2002) defined this term as a factor that predicts symptom persistence versus symptom remission. He further provided a meta-analytic review of risk and maintenance factors involved in eating pathology (Stice,

2002). In his review, he found support for four maintenance factors of eating pathology, although mostly described for those with BN. He describes these factors as a) thin ideal internalization, b) body dissatisfaction, c) negative affect, and d) perfectionism.

In 2003, developers of the cognitive behavioral-maintenance model for BN expanded and enhanced their model to allow it be ‘transdiagnostic’ in nature and to include four additional maintenance factors (Fairburn, Cooper, & Shafran, 2003). According to their new transdiagnostic theory of the maintenance of EDs, one or more of the four additional maintenance factors interact with the original core eating disorder pathology factors (over-evaluation of eating, shape and weight and their control) and this interaction acts as an obstacle to change for certain individuals. The four additional maintenance factors that these authors propose concern: core low self-esteem, interpersonal difficulties, perfectionism, and mood intolerance. In addition, this model was conceptualized to apply to all three major EDs, as AN, BN, and EDNOS are theorized to share the same distinctive psychopathology, and evidence suggests that patients migrate between these diagnostic states over time (Tozzi et al., 2005). Empirical support for this model as a transdiagnostic theory is available in adult populations (Lampard, Byrne, McLean, & Fursland, 2011; Tasca et al., 2011), and in a community-based adolescent sample of binge eating disorder (Allen, Byrne, & McLean, 2012). No research to date has investigated this model in a clinical sample of adolescents with EDs.

Another theory that has been proposed in an attempt to define debilitating EDs that are chronic in nature, is what Robinson (2009) introduces as SEEDS- Serious and Enduring Eating Disorders. A SEED is defined as those with a minimum ED chronicity of 10 years who display ongoing chronic and compromising symptomatology. Robinson

(2009) suggests that there are different subtypes of SEEDS; those who are truly treatment-resistant (i.e. do not respond to treatment), those with chronically low weights and ED related issues but who respond to treatment, and those who experience brief periods of partial remission of symptoms intermingled with multiple serious relapses. Although this term is intended to capture and systematically define those suffering from a chronic ED, to date this term is not widely used in the ED literature, nor has its applicability to youth samples been established due to its duration of illness criteria. Nonetheless, the SEED subcategories are the first attempt in the ED literature to differentiate between different types of refractory EDs. The current project will examine whether it is warranted to subcategorize those with refractory EDs into some of the profiles described above, and if these categories are applicable to youth samples.

Objectives of Current Study

The current project will examine refractory EDs in a large transdiagnostic adolescent sample. It will build on previous work by investigating in a cross-sectional and longitudinal fashion, several biopsychosocial characteristics of refractory EDs in this population. Specifically, this project will explore how characteristics at presentation for an initial intake assessment, progression across the first treatment encounter, and the trajectories over treatment and follow-up periods are related to predicting and understanding refractory EDs in adolescents. In addition, this project will be one of the first to explore a transdiagnostic adolescent sample, which given how prevalent EDNOS is in this age group (Commission on Adolescent Eating Disorders, 2005) provides a much needed comprehensive and generalizable understanding of this entire population. A further aim of this project is to examine more closely the applicability of the additional

maintenance factors (Fairburn et al., 2003) to adolescent refractory EDs, in order to gain a unique view and understanding of how these variables affect the course of refractory EDs in adolescent populations.

In order to achieve these objectives, three studies are proposed. In the first study, the aim is to examine predictors of refractory EDs in an adolescent sample. This study will sequentially explore eleven theoretically-derived predictors of refractory EDs, including those variables identified as the additional maintenance factors in Fairburn's and colleagues (2003) model, for their effect on the occurrence of refractory ED as defined by a return to treatment. The second study will test whether an adolescent transdiagnostic ED sample can be classified into groups or latent classes based on refractory profiles collected at the initial intake assessment or using progress data across the first intensive treatment encounter. This will provide a unique perspective of these refractory profiles, will allow for the exploration of the number of groups that are extracted, and how these indicators classify adolescents with EDs across two different types of data. The ultimate goal of this study is to determine whether a refractory group can be identified from either of these types of data. The third study will explore the growth curves of the additional maintenance factor profiles in a large clinical transdiagnostic sample of adolescents with EDs. The growth curves examined will span across the first treatment encounter and during 6 month and 1 year follow-up periods. Studies examining growth trajectories of these variables have yet to be performed. Examining these curves will allow for the first exploration of how these factors act across treatment and during follow-up in adolescents with and without refractory EDs.

It is anticipated that findings from these three studies will provide important evidence regarding refractory EDs in adolescence. It is anticipated that this project will demonstrate which variables are predictive of a refractory course and whether different types of refractory EDs have empirical support in an adolescent sample. It will further provide information on the role of the additional maintenance variables and their relationship to refractory status, and whether identification of these types of cases is possible based on initial intake and treatment progress data. Results from this line of research could lead to useful information for treatment and prevention efforts concerned with refractory EDs. Clinicians and treatment providers could use this information to better tailor assessment and treatment strategies, so that more effective identification and prevention of refractory EDs can be established.

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Predictors of Refractory Eating Disorders in a Clinical

Sample of Adolescents

Abstract

Eating disorders (EDs) are known as a debilitating group of disorders often described as chronic and relapse-ridden, requiring several rounds of treatment. Identifying predictors of return to treatment, defined as a refractory ED, is crucial to identifying those at risk of a refractory course of illness. The purpose of this study is to examine predictors of refractory versus single-episode EDs in a large clinical sample of adolescents with EDs. Eleven theoretically-derived variables measured at initial intake were examined. Participants in this study were 324 adolescents who received intensive ED treatment at a pediatric tertiary care hospital, where 229 (70.7%) were classified as single-episode and 95 (29.3%) were classified as refractory. A sequential logistic regression was conducted to examine the predictive ability of several ED related variables followed by the contribution of the four additional maintenance factors described in Fairburn and colleagues (2003) transdiagnostic maintenance model. Results indicated that a more acute onset of the ED, higher purging frequency, increased body dissatisfaction, and less depressed mood all significantly contributed to the prediction of refractory status. Further, three of the four maintenance factors; ineffectiveness, interpersonal distrust, and impulsivity also contributed to the prediction of refractory status over and above the initial indicators. Together, these variables significantly predicted refractory EDs with an accuracy rate of 91.7% for the single-episode group and 69.5% for the refractory group. Adolescents at-risk of suffering from a refractory ED can be identified at the initial intake assessment, therefore special attention to this set of indicators should be given.

Predictors of refractory eating disorders in a clinical sample of adolescents

Commonly cited attributes associated with the eating disorders (EDs) are: long-term, chronic, and relapse-ridden (Fairburn et al., 2000; Lewinsohn et al., 2000; Michael Strober, 2004). The cyclical and treatment-resistant nature of these disorders poses, not only, grave long-term physical and mental health risks for the sufferer (Goldstein et al., 2011), it also presents serious challenges for the treating professionals (Strober, 2004), and places a high demand and cost on our health care system (Striegel-Moore, Leslie, Petrelli, Garvin, & Rosenheck, 2000). With gross estimates suggesting that one out of three individuals will suffer from a treatment-resistant course of illness (Richard, Bauer, & Kordy, 2005), the prognosis for those diagnosed with an ED is bleak.

Our ability to identify individuals who might be at risk of poor long-term outcomes in EDs is still in its infancy. This may be due to a lack of clarity on how to operationalize poor long-term outcomes (Bachner-Melman, Zohar, & Ebstein, 2006), relapse and recovery as it applies to the EDs (Quadflieg & Fichter, 2003; Steinhausen, 2002; Walsh, 2008). Although recovery, relapse, and long-term outcomes all vary in definition and operationalization across the ED literature, what is apparent from this literature is that those who return for a second or third course of the same type of treatment (i.e. hospitalization) represent those individuals who have experienced a true relapse, as their symptoms would be considered severe enough to warrant further treatment. Thus, those individuals that require a return to same-type treatment can be clearly defined as having a refractory course of illness.

The term refractory in medical terminology refers to those who are resistant to treatment (US National Library of Medicine, 2012). If an individual requires a second

round of the same-type of treatment, this theoretically equates to treatment resistance. Thus, defining refractory EDs as return to same-type treatment may have benefits to previous incongruent operational definitions, by allowing for the generalizability of this course of illness without complicated definitional terms related to length of symptom abatement/persistence or severity of symptoms. To date, limited work has been conducted that directly relates to identifying predictors of refractory EDs as a return to same-type treatment. Instead, studies and reviews have focused on identifying predictors of relapse or poor treatment outcomes (e.g. Ghaderi, 2010), although notably, most studies have differed in their operationalization of these terms. Although difficult to compare, these reports may lend some initial support for the exploration of these predictors in refractory EDs.

Predictors that have been significantly related to relapse in adult ED patients include presence of purging symptomatology (Baran, Weltzin, & Kaye, 1995; Garner, Garner, & Rosen, 1993; Howard, Evans, Quintero-Howard, Bowers, & Andersen, 1999; Ostuzzi, Didonna, & Micciolo, 1999), lower BMI at time of referral (Hebebrand et al., 1997), longer duration of illness (Howard et al., 1999; Reas, Williamson, Martin, & Zucker, 2000; Richard et al., 2005), later age of onset (Baran et al., 1995), negative attitudes regarding weight and shape (Castro, Gila, Puig, Rodriguez, & Toro, 2004; Richard et al., 2005), and psychiatric comorbidity (Keel & Mitchell, 1997; Pike, 1998; Salbach-Andrae et al., 2009). A recent systematic review of treatment and disease-related outcomes (Berkman, Lohr, & Bulik, 2007) adds three more relevant predictors for those with AN, which are; extreme compulsive drive to exercise, a history of poor social relationships preceding onset of illness, and worse evaluation scores concerning

hypochondrias, paranoia, and psychopathic deviance (Dancyger, Sunday, Eckert, & Halmi, 1997; Strober et al., 1997). The relevance of these constructs in predicting refractory status in adolescent samples has yet to be established, as the developmental appropriateness of these variables have not yet been studied.

In addition, very few studies have explored the utility of these predictors in transdiagnostic samples. Only one study to date has examined predictors in a transdiagnostic adult sample of EDs (McFarlane, Olmsted, & Trottier, 2008), which found evidence for the following significant predictors: severe pretreatment caloric restriction, presence of residual symptoms at discharge, slower response to treatment, and higher weight related self-evaluation (McFarlane et al., 2008). These findings differ somewhat from those predictors found in the AN or BN only adult studies, and also include progress indicators, or indicators of an individuals' progress over treatment. Of the limited studies involving adolescent ED samples, all contain AN or BN samples, and no research examining adolescents who present with a diagnosis of EDNOS, despite the fact that this ED category is most often diagnosed in the adolescent population (Commission on Adolescent Eating Disorders, 2005). With so little evidence available, it is difficult to establish the applicability of these predictors to adolescents with all types of EDs, as it is likely that differences will exist across diagnostic categories and developmental stages.

Little research investigating predictors of refractory EDs in adolescent samples has been performed to date, even though the onset of EDs is known to be frequent during this developmental stage (Pike, 1998; Strober et al., 1997). The few studies conducted in adolescent populations explored predictors of inpatient hospital readmission; with two

recent studies providing some preliminary work investigating refractory EDs as defined by return to treatment. The first of these studies focuses on predictors of rehospitalization after total weight recovery for adolescents with AN (Castro et al., 2004). Findings from this study revealed three significant predictors of readmission; young age (lower than 15 years), abnormal eating attitudes (55 or more on the Eating Attitudes Test), and low rate of weight gain (less than 150 grams per day). However, these results were based on a small total sample of 101 participants, with only 25 (24.8%) of those being identified as requiring readmission. The second study of this nature was a European retrospective multisite project that examined both the course and predictors of rehospitalization in a large sample of 212 AN patients (Steinhausen, Grigoriu-serbanescu, Boyadjieva, Neumarker, & Winkler Metzke, 2008). Results indicated that paternal alcoholism, eating disorder in infancy, periodic overactivity, low weight increase during first admission, and low BMI at first discharge all significantly predicted repeated admissions at an accuracy rate of 69%. Although the latter study builds from the previous, both studies mixed intake assessment and progress variables (i.e. those measured at the end of treatment to assess progress) within the same model, thus limiting their ability to define predictors at the outset of treatment. Further, these studies are limited to patients with AN, and to only one type of treatment modality (hospitalization). Further work in large adolescent transdiagnostic samples involving different types of treatment modalities is needed to fully understand which predictors are involved in adolescent refractory EDs so that more effective identification and treatment of these cases may be possible.

Another line of research relevant to refractory EDs are studies examining maintenance variables. Stice (2002) defined maintenance variables as factors that predict

symptom persistence versus symptom remission. He conducted a meta-analytic review of risk and maintenance factors found to be involved in eating pathology (Stice, 2002), and found support for four maintenance factors for BN pathology: a) thin ideal internalization, b) body dissatisfaction, c) negative affect, and d) perfectionism. In 2003, Fairburn and colleagues (Fairburn, Cooper, et al., 2003) expanded on their original cognitive-behavioral maintenance model for BN (Fairburn et al., 1986) to allow it be transdiagnostic in nature and to include four additional maintenance factors. According to their new transdiagnostic theory, one or more of the four additional maintenance factors (core low self-esteem, interpersonal difficulties, perfectionism, and mood intolerance) interact with the original three core eating disorder pathology factors (over-evaluation of eating, shape and weight and their control) and together they act as an obstacle to change for certain individuals. Based on this theoretical definition, this directly implicates the additional maintenance variables in refractory EDs, warranting further study of the predictive value and impact on refractory EDs.

Further, Fairburn and colleagues (2003) argue that this transdiagnostic maintenance model should apply to all three major EDs, as AN, BN, and EDNOS share similar characteristics. That is, these disorders are theorized to share the same distinctive psychopathology, with evidence suggesting that patients migrate between these diagnostic states over time (Tozzi et al., 2005). The applicability of the additional maintenance variables to understanding and predicting refractory EDs, and the generalizability of this model to transdiagnostic adolescent samples is still unknown. Further testing to explore and expand on the impact of these variables in pediatric

refractory EDs are therefore needed, as this model is one of the first and only theoretically driven, transdiagnostic models applicable to refractory EDs.

The aim of the current study is to explore whether theoretically derived variables measured at the initial intake assessment predict the occurrence of refractory versus single-episode EDs in a large transdiagnostic clinical sample of adolescents. A further aim is to investigate the predictive capabilities of the four additional maintenance factors (proposed in the transdiagnostic maintenance model, Fairburn, Cooper, et al., 2003) to detect refractory EDs, while controlling for the other variables in the model. The ED related variables that will be explored include BMI, self-reported purging frequency, chronicity of symptoms at presentation, drive for thinness, body dissatisfaction, and depressive and anxiety symptoms. Further, based on the additional maintenance factors specified in Fairburn's and colleagues transdiagnostic maintenance model (2003), the variables of perfectionism, interpersonal difficulties, mood intolerance, and core low self-esteem will also be investigated for their predictive value. The current study will explore the ED related variables for their predictive utility in refractory EDs, hypothesizing that each ED related variable will uniquely contribute to the prediction of refractory status in this sample. Next, the additional maintenance factors will be tested for their unique contribution to the prediction of refractory status over and above the ED related variables. If the additional maintenance variables are found to significantly predict refractory status, then support for the role of these variables in adolescent refractory EDs can be established, and preliminary evidence for the utility of the transdiagnostic maintenance in adolescent samples will be available.

Methods

Participants

Participants in this study consisted of 324 adolescent who received specialized inpatient and/or day hospital treatment between January 2000 and January 2011 at the Children's Hospital of Eastern Ontario (CHEO). The overall sample consisted of 307 females (94.8%) and 17 males (5.2%) between the ages of 8 and 18 years, with a mean age of 15.26 years ($SD=1.78$). All youth had a diagnosis of a moderate to severe ED, obtained by a consensus diagnosis delivered by a physician and psychologist/psychiatrist based on DSM-IV-TR criteria (American Psychiatric Association, 2000). Just over half (54.8%) of the sample was diagnosed with AN, 11.9% of the sample was diagnosed with BN, and exactly one third of the sample (33.3%) was diagnosed with EDNOS. Data retained for use in this study consisted of participants who met criteria for a refractory or single-episode ED. Refractory EDs were operationally defined as those adolescents who returned for a second course of the same type of intensive treatment or who returned for a more intensive level of treatment (i.e. completed day treatment and returned for specialized intensive inpatient treatment). Single-episode cases were defined as those patients who only received one recommended treatment dose. Those patients who received outpatient services exclusively were excluded from all analyses.

Description of Eating disorder program

Participants of this study consisted of individuals who were treated by the regional ED program located at the Children's Hospital of Eastern Ontario. The population treated includes children and adolescents aged 8 to 18 years from across the province, serving a population of approximately 1.5 million. Patients are referred through

three channels, either via their family physician, the local emergency department, or through a provincial network. Two specialized group-based intensive programs are offered: Inpatient or Day Hospital services. Both programs are group-based integrated programs primarily based on Maudsley family-based treatment (FBT) principles (Lock & Fitzpatrick, 2007), wherein the parents are empowered to support their child in recovery. The program also incorporates some components of cognitive-behavioural treatment, dialectical behaviour therapy, interpersonal therapy, mindfulness, expressive arts therapy, pet therapy and yoga.

Day Hospital Program. The Day Hospital Eating Disorder Program has been in operation since 2000, and represents the first specialized partial hospitalization treatment program offered in the region. The program has a maximum capacity of 8 youth, and operates from 8am to 6pm 5 days per week. The typical length of program is 12 to 14 weeks, and approximately 35 patients are treated each year. During the course of the program, all recipients receive group therapy, meal support, academic support, therapeutic outings, and individual and family therapy. This program is often used as a step-down treatment plan for those who successfully complete the inpatient program.

Inpatient Program. Since the formal opening of the program in January of 2007, the Inpatient Eating Disorder program has treated approximately 45 to 55 children and youth each year, with average lengths of stay ranging from 30 to 60 days. This group-based treatment program has six inpatient beds, allocated on a shared child psychiatric ward of a local tertiary care pediatric hospital. The main goal of the specialized inpatient program is medical stabilization, although normalization of eating, nutritional

rehabilitation, and reduction of comorbid symptoms is also a focus. Individual and FBT are also essential to the inpatient program.

Assessment Measures

Demographic data. The demographic variables age, gender, BMI, diagnosis, treatment modality, and chronicity of illness at initial intake assessment were collected from clinical charts.

Children's Depression Inventory (CDI; Kovacs, 1985, 1992). The CDI is a 27-item, validated self-report questionnaire assessing cognitive, affective, and behavioral variables related to depression in children and adolescents. It is valid for youth between 7 and 17 years of age (Kovacs, 1992). The questionnaire yields five subscales and a total score. Overall, the CDI demonstrates good psychometric properties and sensitivity to clinical changes in depressive symptoms over time (Kovacs, 1992; Smucker, Craighead, Craighead, & Green, 1986). It has been established as internally consistent and valid in both clinical and non-clinical samples of adolescents (Kovacs, 1992; Smucker et al., 1986), with internal consistency scores in the current samples estimated at .920 for the total score. Norms and clinical cut-offs for this scale are derived based on t-scores, wherein t-scores of 50 to 64 are considered in the normal to borderline range, and t-scores of 65 or greater are indicative of clinical levels of depressed mood. Only the CDI total score and corresponding t-score will be retained for use in this study.

Multi-dimensional Anxiety Scale for Children (MASC; March, 1997). The MASC is a 39-item self-report questionnaire measuring anxiety related symptoms in children between 8 and 19 years of age (March, 1997). The questionnaire yields four scales, three indices, and six subscales. Overall, the MASC yields good psychometric

data, good internal consistency (March, Parker, Sullivan, Stallings, & Conners, 1997), and is sensitive to clinical changes in anxiety related symptoms over time (March, 1997). It has demonstrated good internal consistency properties in the current sample with an alpha coefficient of .922 for the total score. Norms and clinical cut-offs for this scale are derived based on t-scores, wherein t-scores of 50 to 64 are considered in the normal to borderline range, and t-scores of 65 or greater are indicative of clinical levels of anxiety. Only the total score and corresponding t-score will be examined in this study.

Eating Disorder Inventory – 2 (EDI-2; Garner, 1991). The EDI-2 provides a comprehensive assessment of the behavioral and psychological dimensions characteristic of EDs. The EDI-2 is a reliable and valid 91-item multidimensional self-report instrument that assesses characteristics of EDs, with higher scores indicating more severe symptomatology and/or more pathological attitudes and cognitions. The EDI-2 is divided into 11 subscales and has been found to have good psychometric properties. The specific subscales and corresponding internal consistency values (derived from an adult clinical ED sample of women aged 14 to 55 years) for those indices to be used in the current study are: Drive for Thinness (.81), Body Dissatisfaction (.91), Perfectionism (.80), Impulse Regulation (.75), Ineffectiveness (.87) and Interpersonal Distrust (.82)(Eberenz & Gleaves, 1994). These values provide evidence of good internal consistency for those subscales to be used in the current study. Possible ranges for these subscale scores are presented in Table 1. As has been done in previous studies (Tasca et al., 2011), the additional maintenance model construct of mood intolerance will be measured using the Impulse Regulation subscale, the construct of core low self-esteem will be measured

using the Ineffectiveness subscale, and the construct of interpersonal difficulties will be measured using the Interpersonal Distrust subscale score.

Purging Frequency. To obtain a frequency of purging behavior for use in this study, the combination of items from two different self-report measures was employed. This is because prior to 2007, the Eating Disorder Inventory – Symptom Checklist (EDI-SC; Garner, 1991) was used to establish self-reports of ED related behaviors and symptoms. In this questionnaire, the item ‘How many times over the past month did you vomit’ was used to establish frequency over a one-month period. After 2007, self-reports of ED symptoms were established using the Eating Disorder Examination Questionnaire for Adolescents (EDEQ-A; Carter, Stewart, & Fairburn, 2001). Question 17 of the measure asks respondents to indicate the number of times the individual has vomited over the past 2 weeks for the purposes of losing weight. In order to have one measure of purging frequency, the monthly estimates from the EDI-SC were divided by two and then merged with the EDEQ-A scores to create a frequency measure of purging across a 2-week span. Although no evidence exists that supports the accuracy or validity of this method to obtain an estimate of purging frequency, self-report measures of frequency of symptoms are almost always retrospective and therefore open to more reporting error. Thus, combining these reports in this fashion was not considered a threat to the integrity of this data.

Procedures

This study consists of secondary use of clinical data retrieved with permission from the Eating Disorder Program at CHEO. One of the clinical components of the program is the use of psychometric measures to aid in evaluating the patient’s recovery

over time. Batteries of clinically useful measures are administered to the patients at various intervals throughout each treatment session in order to help in understanding patients' needs. Only measures administered at the initial intake assessment were retained for use in the current study. The Research Ethics Boards at the Children's Hospital of Eastern Ontario and at the University of Ottawa approved this study.

Analytic Plan

A sequential binomial logistic regression analysis was used to test the model that best predicts refractory EDs in this sample. The logistic regression analysis was performed on the outcome variable refractory status (single-episode = 0; refractory = 1), with eleven variables being used to predict group membership. The predictors were entered in sequential order, first on the basis of the main ED related variables (chronicity of ED, BMI at assessment, purging frequency over 2 week period, drive for thinness, body dissatisfaction, depression scores, and anxiety scores), and next with the four additional maintenance variables (perfectionism, ineffectiveness, interpersonal distrust, impulsivity) from Fairburn's and colleagues model (2003). This allowed for the testing of the predictive capabilities of the ED related variables alone, followed by the contribution of the additional maintenance factors on the detection of refractory EDs. A Bonferroni correction was used due to the number of predictors in the model, thus a Type I error rate of 0.0045 (.05/11) was applied.

Results

The sample in this study consisted of 324 adolescents who presented for a comprehensive assessment between June 2000 and January 2011. Of the 324 patients who received intensive treatment, 229 (70.7%) were classified as single-episode cases, or

those adolescents who only received one round of intensive services, and 95 (29.3%) adolescents were classified as refractory cases, or those who received two or more rounds of intensive services. The refractory group contained almost exclusively females ($n=94$, 98.9%), and the number of treatment encounters ranged from a minimum of 2 courses of intensive treatment to a maximum of 6 rounds of intensive treatment. Table 1 presents the descriptive information for the eleven predictors separated by refractory status.

Predicting Refractory Status

Results of the sequential logistic regression analysis revealed a good model fit for the ED related variables [$\chi^2 (7, N = 324) = 103.39, p < .001$]. Based on the seven ED related variables, the single-episode group could be predicted at a 91.3% accuracy rate, and the refractory group could be predicted at a 57.9% accuracy rate. The model with both the ED related variables and the four additional maintenance variables also demonstrated good model fit, with a log-likelihood difference test revealing that model 2 was reliably different, and its addition provided a statistical improvement to model 1 [$\chi^2 (4, N = 324) = 60.931, p < .001$]. With the addition of the four additional maintenance variables, the overall model was able to significantly predict 91.7% of the single-episode group and 69.5% of the refractory group. Additionally, the Hosmer & Lemeshow goodness of fit tests were non-significant for both blocks of the model, providing further evidence that the set of predictors are adequate at classifying refractory status. The Nagelkerke measure of strength of association increased with the addition of the second block of predictors, resulting in all 11 variables accounting for 56.7% of the prediction of refractory status.

Table 2 displays regression coefficients, Wald statistics, odds ratios and 95%

confidence intervals for the eleven predictors included in the full model. Four of the seven ED related predictors, and three of the four additional maintenance factors uniquely and significantly contributed to the prediction of refractory status in this sample, while controlling for the effects of the other variables in the model. The odds ratios obtained in this analysis suggest that for every additional month of chronicity endured prior to presenting for an initial intake ED assessment, the odds that the individual will experience a refractory course versus a single-episode course are decreased by 25.6%. The odds of having a refractory ED are increased by 25.1% for each additional purging episode that is experienced in a 2-week period, and by 22.4% for every one unit increase in body dissatisfaction that is experienced. Contrary to what would be expected, the odds that an individual will experience a refractory course are decreased by 15% for every one unit increase in depressed mood that is reported.

According to the analysis of the additional maintenance variables, ineffectiveness, interpersonal distrust and impulse dysregulation all significantly contributed to the prediction of refractory status over and above the contributions of the ED related variables. The odds of experiencing a refractory course of illness are increased by 18.0%, 26.1% and 8.3% respectively with every one unit increase in ineffectiveness, interpersonal distrust and impulse dysregulation reported by the individual. Perfectionism did not emerge as a significant predictor. Taken together, these results suggest that higher frequency of purging behaviour, shorter chronicity, higher body dissatisfaction, and less depressed mood reliably predicts refractory status. Adding to this, higher ineffectiveness, interpersonal distrust, and impulse dysregulation also add to the prediction of the refractory status while taking into account the other ED related variables, declaring the

importance of these additional maintenance variables in being able to differentiate between those adolescent ED patients who are classified as single-episode versus refractory.

Being able to differentiate between those patients who will have a refractory versus a single-episode course could allow for the development of treatment plans that are better tailored to suit the needs of the refractory sufferer. This could lead to more effective first courses of treatment, and could result in less need for repetitive intensive treatment courses. An increase in treatment effectiveness could result in decreased costs for the patient and the healthcare system, and allow for these savings to be redirected to treating more youth who currently fail to receive recommended services due to a lack of treatment resources. Thus, early identification of refractory status yields important clinical information for treatment interventions and decisions.

Discussion

The focus of the present study was to examine predictors of a refractory course of an ED in a large transdiagnostic sample of adolescents with EDs, based on characteristics measured at the initial intake assessment. To date, the literature examining predictors of refractory EDs is limited, and is even more limited for adolescent populations, which provides little guidance as to which characteristics when present, are able to identify those who are at risk of suffering from a refractory ED.

In the large transdiagnostic sample of adolescents with EDs explored in this study, approximately 30% were classified as refractory based on the definition of return to treatment. This is consistent with some past adult studies of clinical EDs (Richard et al., 2005). Although adolescent studies have estimated prevalence rates of

rehospitalization to be between 24.8% and 44.8% (Castro et al., 2004; Steinhausen et al., 2008), these studies have been limited to only those suffering from AN and to inpatient treatments only. Thus, prevalence rates obtained from this study are more generalizable to adolescents with any type of ED who undergo various types of intensive treatments (i.e. inpatient and/or day hospital programs). Results found in this study indicated that approximately 1 in 3 adolescents, who initially require intensive treatment for their ED, will experience a refractory course. Based on these rates, much attention should be given to better identifying potential refractory cases at the point of entry into the mental health system, so that early identification and refined treatments geared towards those factors that maintain the illness could be applied.

Results from this study suggest that variables assessed at the initial intake can significantly identify those individuals who are likely to suffer from a single-episode versus refractory course of an ED. Further, this study demonstrated that the additional maintenance variables added significant predictive value to refractory status over and above the ED related predictors. Of the eleven predictors examined in a sequential model, the combination of seven of the indicators uniquely contribute to the successful prediction of refractory status at an accuracy rate of approximately 70%.

Chronicity of illness emerged as a unique significant predictor, with shorter chronicity (or more acute onset) predictive of refractory status. Although adult studies have alluded to longer chronicity being a risk factor for refractory EDs (Howard et al., 1999; Reas et al., 2000; Richard et al., 2005), the findings in this study suggest the opposite. This result is most likely reflective of developmental differences concerning this construct in refractory EDs. In an adolescent sample, having a severe, acute onset of

an ED that leads to an assessment at a tertiary care facility may indicate a greater severity of illness and a likelihood of a refractory course of illness. This could also be understood in terms of those with a more acute onset of the disorder being at greater risk of suffering from a refractory course of illness, as those who get severely ill very quickly may in fact represent a more at-risk group. This finding indicates developmental differences exist with this variable and its relation to refractory EDs, and therefore speaks to the importance in studying the developmental appropriateness of those factors thought to be involved in refractory EDs.

Another significant predictor that emerged from this study was frequency of purging behavior, which is in line with some previous studies (Baran et al., 1995; Garner et al., 1993; Howard et al., 1999; Ostuzzi et al., 1999). The current study provides further evidence that greater purging frequency is a risk factor of a refractory course of illness, and that the greater the frequency of purging behaviors, the greater the risk of experiencing a refractory course. Clinicians should pay special attention to those patients who present with severe purging behaviour as this may be a sign that a refractory ED is present.

In terms of ED related cognitions, body dissatisfaction emerged as another significant unique predictor of refractory EDs, with those experiencing greater dissatisfaction with their bodies, representing those who might be at greater risk of experiencing a refractory course of an ED. This in line with previous work performed in adult samples of AN and BN samples (Keel et al., 2005). Treatment attempts aimed at shifting or alleviating body dissatisfaction may be helpful in reducing the number of treatment encounters necessary to resolve the refractory ED.

Further findings of the current study suggest that three of the four additional maintenance factors uniquely and significantly add to the predictability of refractory illness, after taking into account the other ED related variables in the model. The additional maintenance variables of ineffectiveness, interpersonal distrust and impulse dysregulation all emerged as unique significant predictors of refractory status, while perfectionism was not found to be significantly related. The inclusion of the additional maintenance variables significantly strengthened the predictive abilities of the model, allowing for an increase of 11.6% in accuracy rates for successful prediction of refractory cases. This provides further evidence of the predictive strength of the majority of the additional maintenance variables to predict refractory EDs, and adds merit to the role of these in Fairburn's and colleagues theory (Fairburn, Cooper, et al., 2003).

These results also provide one of the first accounts of the generalizability of these factors to an adolescent sample. It demonstrated that regardless of age, ineffectiveness, interpersonal distrust and impulse dysregulation are factors that are related to maintaining an ED. The finding that perfectionism was not significantly related to the prediction of refractory status, confirms findings of one adult study for BN samples (Tasca et al., 2011), yet contradicts the proponents of the maintenance model (Fairburn, et al., 2003). This adds merit to testing the developmental appropriateness of these model constructs. Further studies of perfectionism in this theoretical model across different age groups are still needed to fully understand whether this construct is related to the maintenance of EDs.

Another surprising findings that emerged was that higher depressed mood decreased the chances of having a refractory ED. As the causal relationship between

depression and eating disorders is still under debate (Wall, Cumella, & Lafferty O'Connor, 2008), it may be that those who present with elevated levels of depressed mood represent those ED patients whose eating disorder is more about the depression than it is the ED. That is, for these individuals, once the depressive symptoms are lifted via means of treatment, the ED symptoms may then easily dissipate, as they were primarily present due to the concurrent depressive symptoms. It could also be the case that the depression inventory used in this study (CDI; Kovacs, 1992) measures level of distress, and that some level of distress is necessary to be motivated for ED treatment. This finding may also be a result of developmental artifact, wherein only in adolescent samples does more severe depressed mood make an individual less likely to experience a refractory ED. Other possible reasons for this finding is that adolescents with increased depressed mood may be those cases who are less in denial of their ED, therefore more accurately reporting feelings of low mood, or that their symptoms are no longer numbing the depression, creating more motivation for change. Further research exploring this relationship in adolescent samples is needed to better understand this finding.

One of the limitations of this study was the sole use of self-report questionnaires. Triangulation of data from multiple sources (i.e. parents, teachers) could enhance the reliability of the predictors. Additionally, the operational definition of a refractory ED as a return to treatment may have hindered some of the results, as it was not possible to account for individuals who returned to treatment in the adult system, who sought treatment at a different location or in the community, or those who did not return for treatment when it was recommended by the team. However, the operationalization of a refractory ED as a return to treatment did overcome the past problems with the definition,

and provided a more reliable and valid method of identifying those who are truly refractory.

Future studies should explore whether defining refractory EDs as a return to treatment continues to provide a reliable method of identifying a group of adolescents who do not benefit from their first treatment course for an ED. Also, studies examining the predictive nature of the maintenance model in the different diagnostic categories separately and in male samples would also be beneficial. Further, examining post-treatment predictors or change score predictors, as has been performed in adult studies, may also be informative. Lastly, examining the maintenance model and its predictive ability over time would also serve to help us better understand how it truly maintains the ED, thus longitudinal studies of this nature would be a large contribution to this field.

The ability to better predict refractory EDs, and to identify at initial intake those who are at risk for a refractory course of an ED could have a significant impact on the patient and their family, the treatment team that must invest heavily into the individuals care, and to the healthcare system as a whole. Identification of factors that significantly maintain the disorder is crucial, as once researchers and clinicians can pinpoint these factors, they can provide more effective treatments designed to address maintenance or refractory constructs. Findings from this study demonstrate that these variables are a reliable set of predictors that can help determine who may experience a refractory ED; therefore, assessment of these characteristics should be incorporated into clinical assessment and treatment recommendations. Administering and incorporating this set of predictors into regular initial intake assessments can help identify, at intake, those individuals who are at risk of a refractory ED, and can help focus treatment efforts to

target these factors. With the peak onset of EDs occurring during adolescence (Bryant-Waugh, 2006), it is essential to be able to identify and treat refractory EDs in youth, as the long-term effects of refractory EDs is likely to spill into adulthood, and carries with it heavy costs and long-term mental and physical consequences.

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Table 1. Means (SD) and reported ranges for all predictors separately for single-episode and refractory groups

	Single episode (n=229)		Refractory (n=95)		Possible range
	Mean (SD)	Reported range	Mean (SD)	Reported range	
ED Related Variables					
Chronicity of ED (months)	18.97 (15.12)	3 – 66	11.57 (8.42)	1 – 40	--
Body Mass Index (kg/m ²)	18.17 (3.07)	12.4 – 27.3	17.20 (2.64)	12.8 – 28.0	--
Purging frequency	11.21 (11.17)	1 – 45	13.34 (12.39)	1 – 42	--
Drive for Thinness	12.49 (7.59)	0 – 21	14.88 (6.77)	0 – 21	0 – 21
Body Dissatisfaction	14.40 (9.53)	0 – 27	17.41 (9.29)	0 – 27	0 – 28
Depressed Mood (t-score)	65.68 (18.12)	34 – 100	67.87 (18.28)	34 – 100	34 – 100
Anxiety (t-score)	58.97 (12.57)	28 – 87	59.97 (11.58)	36 – 90	25 – 100
Maintenance Variables					
Perfectionism	7.17 (4.69)	0 – 18	6.69 (4.87)	0 – 18	0 – 18
Ineffectiveness	10.46 (8.72)	0 – 28	11.93 (9.13)	0 – 28	0 – 28
Interpersonal Distrust	5.25 (4.59)	0 – 18	5.92 (4.75)	0 – 17	0 – 18
Impulsivity	5.98 (6.14)	0 – 27	7.51 (7.35)	0 – 27	0 – 27

Table 2. Sequential logistic regression of refractory status predicted by ED related and maintenance variables (n=324)

	<i>B</i>	Wald χ^2 (<i>p</i> value)	Odds Ratio	95% CI for Odds Ratio		Model χ^2 (<i>p</i> value)	-2 Log likeliho od	Hosmer & Lemeshow χ^2 (<i>p</i> value)	Nagel- kerke R ²
				Lower	Upper				
Block 1: ED related						103.39 (.000)	288.65	3.13 (.926)	.389
Chronicity of ED	-.295	58.80 (.000)	.744	.690	.803				
BMI	-.145	2.41 (.120)	.865	.721	1.039				
Purging frequency	.224	45.52 (.000)	1.251	1.172	1.335				
Drive for Thinness	-.061	1.78 (1.82)	.941	.860	1.029				
Body Dissatisfaction	.203	22.33 (.000)	1.224	1.126	1.332				
Depressed Mood	-.162	30.61 (.000)	.850	.803	.901				
Anxiety	.036	3.42 (.065)	1.036	.998	1.077				
Block 2: Maintenance						60.93 (.000)	227.72	12.12 (.146)	.567
Perfectionism	-.094	4.46 (.035)	.911	.835	.993				
Ineffectiveness	.165	10.74 (.001)	1.180	1.069	1.302				
Interpersonal Distrust	.232	16.89 (.000)	1.261	1.129	1.409				
Impulsivity	.201	17.20 (.000)	1.222	1.112	1.344				

Bonferroni correction applied: $p = .05/11 = .0045$

Identifying Profiles of Refractory Cases in Adolescents with Eating Disorders:

A Latent Profile Analysis

Abstract

Eating disorders (EDs) are repeatedly described as chronic, and are known to have their onset during adolescence. Identifying profiles of those adolescents at risk of suffering from a chronic ED is currently not possible. Similarly, our knowledge of the profiles or groups of refractory EDs- or those EDs that require two or more intensive treatment courses, is also very limited. The objective of the current exploratory study was to examine whether adolescents can be classified into groups based on a number of factors theoretically associated to refractory EDs, and whether indicators at initial assessment or pre to post the first treatment encounter, are able to differentiate between profiles. For the first analysis 324 adolescents participated, whereas data from 234 adolescents were available for the second analysis (had both pre and post data available). Results of the first profile analysis revealed that three groups do exist when examining ED related and additional maintenance characteristics at initial intake, but that no emerging group represented a refractory group. Findings of the second analysis also revealed a 3-class solution that best fits the data, and that one of the groups from the emerging classification was statistically related to the refractory group, establishing that progress indicators can reliably distinguish a refractory group. Results of this study suggest that when examining ED related and additional maintenance variables either at initial intake or across the first treatment encounter, three types of profiles seem to exist. The ability to distinguish a refractory course of illness based on patient profiles is possible using progress indicators, thus clinicians should place more weight on how an adolescent with an ED responds to treatment during their first treatment encounter as an indicator of a possible refractory ED, versus those characteristics reported at the initial intake assessment.

Identifying Refractory Eating Disorders in Adolescents:

A Latent Profile Analysis

Studies have shown that adolescents diagnosed with an eating disorder (ED) face a lifelong battle with their eating problems (Kruger et al., 19998; Lask et al., 1997). This battle pulls the adolescent far from the normative developmental trajectory, and accompanies with it many physical, psychological, and social consequences (Pike, 1997; Reijonen, 2003). For this reason, EDs have been described as being ‘high-priced’ both in terms of healthcare dollars and in mortality rates (Krauth, Buser, & Vogel, 2002; Simon, Schmidt, & Pilling, 2005; Striegel-Moore, Leslie, Petrill, Garvin, & Rosenheck, 2000). With adolescence representing the peak onset for an ED (Reijonen, 2003), and with long-term outcome studies reporting recovery rates as low as 57% at 10-year follow-up (Steinhausen, 2002), the apparent need to understand adolescent-onset EDs and their outcomes is imminent.

Identifying individuals at risk of suffering from a long course of an ED is currently not possible. This may in part be due to the lack of consensus across clinicians and researchers on how to define poor long-term outcomes, relapse and recovery as it applies to the EDs (Quadflieg & Fichter, 2003; Steinhausen, 2002; Walsh, 2008). Although recovery, relapse, and long-term outcomes all appear to vary in definition and operationalization across the ED literature (Quadflieg & Fichter, 2003; Steinhausen, 2002; Walsh, 2008), what is certain is that those who return for a second or third course of the same type of treatment represent those cases who have truly experienced a relapse. In other words, those individuals who require a return to same-type treatment could qualify as those who have a refractory course of illness.

The term refractory in medical literatures refer to those whose symptoms are resistant to treatment (US National Library of Medicine, 2012). If an individual is recommended to undergo a second round of a similar-type treatment, this can be equated to symptom resistance or presence of a refractory ED. The ability to identify those individuals that may be at risk of a refractory course, as well as the ability to profile these individuals in terms of psychopathology and psychosocial functioning, may have several clinical benefits. Specifically, the ability to tailor and apply specialized interventions to the most at-risk group of refractory ED cases could potentially alter and shorten the duration of a refractory course of illness.

Currently, our knowledge of the profiles of those who might be at risk of a refractory course of an ED is limited. Similarly, possible indicators or factors involved in a refractory ED also remain inconsistent due to definitional and methodological issues (Richard, Bauer, & Kordy, 2005). Depending on the terminology used to describe this course of illness, differing variables have been found to predict refractory EDs. For example, a large review of poor long-term treatment outcomes of EDs (Ghaderi, 2010) point to some predictors that might be implicated in refractory cases. Similarly, studies examining predictors of hospital re-admission (e.g. Castro et al., 2004) or relapse (e.g. Salbach-Andrae et al., 2009) also provide some pertinent variables to examine when exploring refractory EDs. Although these types of studies provide some evidence of significant predictors of refractory EDs, they all differ in their terminology and operationalization of the outcome variable, making it difficult to build strong evidence of any one predictive profile. Another issue is that some studies have investigated predictors that are collected at the initial intake assessment, whereas other studies have looked at

progress or change predictors, that is predictors that are based on the change that has occurred between two time points (e.g. between pre and post treatment). The difference between these two types of data makes it difficult to combine the findings of the various studies to establish a concrete profile of refractory EDs. It also makes it difficult for practitioners to know which variables to pay attention to for the detection of a refractory course of illness.

Some of the key variables that have been demonstrated to be related to refractory EDs relate to purging symptomatology (Baran, Weltzin, & Kaye, 1995; Garner, Garner, & Rosen, 1993; Howard, Evans, Quintero-Howard, Bowers, & Andersen, 1999; Ostuzzi, Didonna, & Micciolo, 1999), lower BMI at time of referral (Hebebrand et al., 1997), longer duration of illness (Howard et al., 1999; Reas, Williamson, Martin, & Zucker, 2000; Richard et al., 2005), later age of onset (Baran et al., 1995), negative attitudes regarding weight and shape (Castro et al., 2004; Richard et al., 2005), and psychiatric comorbidity (Keel & Mitchell, 1997; Pike, 1998; Salbach-Andrae et al., 2009).

Similarly, some of the progress or change predictors that have been found to be related to refractory EDs involve the presence of residual symptoms at discharge, slower response to treatment (McFarlane, Olmsted, & Trottier, 2008), low BMI at discharge and insufficient weight gain over the course of hospitalization (Castro et al., 2004; Howard et al., 1999; Lay, Jennen-Steinmetz, Reinhard, & Schmidt, 2002; Ostuzzi et al., 1999). The ability to distinguish a refractory course of illness based on patient characteristics at initial intake versus progress indicators across treatment has yet to be established. Both types of characteristics provide vital information for the treating professionals. Whether

these types of information can be useful to identify individuals at risk of a refractory course of illness still warrants further investigation.

Maintenance variables, or factors that predict symptom persistence versus symptom remission (Stice, 2002) are also relevant to refractory EDs. Thin ideal internalization, body dissatisfaction, negative affects, and perfectionism have all been identified as variables thought to play a role in maintaining an ED (Stice, 2002). Similarly, a recent theoretical maintenance model of EDs proposed by Fairburn and colleagues in 2003 (Fairburn, Cooper, et al., 2003) also contained maintenance factors. According to their new transdiagnostic theory, one or more of the four additional maintenance factors (core low self-esteem, interpersonal difficulties, perfectionism, and mood intolerance) interact with the original three core eating disorder pathology factors (over-evaluation of eating, shape and weight and their control) and together they act as an obstacle to change for certain individuals who experience severe or problematic ED symptoms, leading to persistent or maintained EDs.

In terms of identifying and classifying different types of persistent EDs, Robinson (2009) introduces what he labels SEEDS- Serious and Enduring Eating Disorders. A SEED is defined to capture those with a minimum ED chronicity of 10 years and those who are characterized with having chronic and compromising symptomatology. Robinson (2009) suggests that there are different subtypes of SEEDS; those who are truly treatment-resistant, those with chronically low weights and ED related issues yet respond to treatment, and those who experience brief periods of partial remission intermingled with multiple serious relapses. Although this term is intended to capture and systematically define those suffering from a refractory ED, to date this term is not widely

used in the ED literature, nor is the applicability to youth samples been tested.

Nonetheless, the SEED subcategories are the first attempt in the ED literature to differentiate between different types of refractory cases. An empirical study to validate these categories has yet to be performed in either adult or adolescent samples.

Based on the theory found in Stice's (2002) maintenance variables, Fairburn and colleagues (2003) transdiagnostic maintenance model, and Robinson's SEEDS groupings (2009), it is plausible that three different ED groups exist; those who are single-episode, those characterized by cyclical periods of remission followed by relapses, and those who are identified as having chronically low weights and continuous ED related issues.

Whether these grouping are detectable at initial intake assessment or based on progress indicators across the first treatment encounter is one of the main focuses of the current study.

Identifying subsamples of individuals within a certain population has a multitude of implications and benefits. Primarily, it can help develop better interventions more directly targeted to the specific subsample, and it could also aid with the specific reach and effectiveness of future interventions (Mailey et al., 2012). Several statistical methodologies are able to identify subgroups of individuals based on behavioral profiles or characteristics of the individual. Latent profile analysis (LPA), also known as latent class cluster analysis (LCCA) is one of these techniques that identifies unique subgroups based on the profiles of continuous indicators of interest (Vermunt & Magidson, 2002).

Within the field of EDs, several classification studies have been performed, mostly with the intent of refining the nosology or phenotypes of EDs. For example, an LPA has been performed to classify ED diagnosis in both clinical (e.g. Eddy et al., 2010;

Holle et al., 2008; Keel et al., 2004) and community-based samples (e.g. (Duncan et al., 2007), and classification of EDNOS phenotypes (Mitchell et al., 2007), and phenotypes based on personality traits (Krug et al., 2011) and ED symptoms (Bulik, Sullivan, Fear, & Pickering, 2000) have also been conducted. Very limited profile research has been performed in adolescent samples of EDs, and no studies have attempted to examine profiles of ED related and maintenance factors in either adult or adolescent samples.

The objective of the current exploratory study is to examine whether adolescents can be classified into groups based on a number of continuous psychological, psychosocial and additional maintenance factors theoretically associated to refractory EDs. Further, this study aims to investigate whether the classification that does emerge permits for the identification of a distinct refractory group. As indicators of refractory status have previously been based on both initial assessment data and on progress scores across treatment, two LPAs are proposed in order to investigate whether each type of data can reliably identify distinct profiles of pediatric refractory EDs. The first LPA will concern data collected at the initial intake assessment, whereas the second LPA will examine pre to post data across the first treatment encounter.

To accomplish the objectives in this study, several steps were performed for each data type examined (initial intake assessment data and change score data across the first treatment course). In both data sets, the first step was to explore how many groups emerged based on the set of variables included in the analysis. The next step was to examine whether the emerging groups or profiles clearly distinguish a refractory subgroup. This includes statistically testing whether differences exist amongst the emerging profiles. Further, and in order to confirm whether a refractory group is

detectable either at initial intake or based on pre to post change scores, a comparison of the emerging groups against refractory status as defined by a return to same-type treatment was examined.

Methods

Participants

Participants for this study consisted of 324 adolescent ED patients who received specialized inpatient and/or day hospital treatment between January 2000 and January 2011 from a tertiary care hospital located in Ottawa, Canada. The overall sample consisted of 307 females (94.8%) and 17 males (5.2%) between the ages of 8 and 18 years, with a mean age of 15.26 years ($SD=1.78$). All youth had a diagnosis of a moderate to severe ED, obtained by a consensus diagnosis delivered by a physician and psychologist/psychiatrist based on DSM-IV-TR criteria (American Psychiatric Association, 2000). Just over half (54.8%) of the sample was diagnosed with AN, 11.9% of the sample was diagnosed with BN, and exactly one third of the sample (33.3%) was diagnosed with EDNOS. Data retained for use in this study consisted of participants who met criteria for a refractory ED or who were considered single-episode. Refractory EDs are operationally defined as all adolescents who return for a second course of the same type of intensive treatment or return to a more intensive level of treatment (i.e. complete day treatment and return for inpatient treatment). Single-episode cases are defined as those patients who have received only one recommended treatment dose. Both initial assessment and pre to post data collected over the course of the first treatment encounter were used in the current study.

Description of Eating disorder program

Participants of this study consisted of individuals who were treated by the regional ED program located at the Children's Hospital of Eastern Ontario. The population treated includes children and adolescents aged 8 to 18 years from across the province, serving a population of approximately 1.5 million. Patients are referred through three channels, either via their family physician, the local emergency department, or through a provincial network. Two specialized group-based intensive programs are offered: Inpatient or Day Hospital services. Both programs are group-based integrated programs primarily based on Maudsley family-based treatment (FBT) principles (Lock & Fitzpatrick, 2007), wherein the parents are empowered to support their child in recovery. The program also incorporates some components of cognitive-behavioural treatment, dialectical behaviour therapy, mindfulness, expressive arts therapy, pet therapy and interpersonal therapy.

Day Hospital Program. The Day Hospital Eating Disorder Program has been in operation since 2000, and represents the first specialized partial hospitalization treatment program offered in the region. The program has a maximum capacity of 8 youth, and operates from 8am to 6pm 5 days per week. The typical length of program is 12-14 weeks, and approximately 35 patients are treated each year. During the course of the program, all recipients receive group therapy, meal support, academic support, therapeutic outings, and individual and family therapy. This program is often used as a step-down treatment plan for those who successfully complete the inpatient program.

Inpatient Program. Since the formal opening of the program in January of 2007, the Inpatient Eating Disorder program has treated approximately 45 to 55 children and

youth each year, with average lengths of stay ranging from 30 to 60 days. This group-based treatment program has six inpatient beds, allocated on a shared child psychiatric ward of a local tertiary care pediatric hospital. The main goal of the specialized inpatient program is medical stabilization, although normalization of eating, nutritional rehabilitation, and reduction of comorbid symptoms is also a focus. Individual and FBT are also essential to the inpatient program.

Assessment Measures

Demographic data. The demographic variables age, gender, BMI, diagnosis, treatment modality, and chronicity of illness at assessment were collected from clinical charts.

Children's Depression Inventory (CDI; Kovacs, 1985, 1992). The CDI is a 27-item, validated self-report questionnaire assessing cognitive, affective, and behavioral variables related to depression in children and adolescents. It is valid for youth between 7 and 17 years of age (Kovacs, 1992). The questionnaire yields five subscales and a total score. Overall, the CDI demonstrates good psychometric properties and sensitivity to clinical changes in depressive symptoms over time (Kovacs, 1992; Smucker, Craighead, Craighead, & Green, 1986). It has been established as internally consistent and valid in both clinical and non-clinical samples of adolescents (Kovacs, 1992; Smucker et al., 1986), with internal consistency scores in the current sample estimated at .920 for the total score. Norms and clinical cut-offs for this scale are derived based on t-scores, wherein t-scores of 50 to 64 are considered in the normal to borderline range, and t-scores of 65 or greater are indicative of clinical levels of depressed mood. Only the CDI total score and corresponding t-score will be retained for use in this study.

Multi-dimensional Anxiety Scale for Children (MASC; March, 1997). The MASC is a 39-item self-report questionnaire measuring anxiety related symptoms in children between 8 and 19 years of age (J.S. March, 1997). The questionnaire yields four scales, three indices, and six subscales. Overall, the MASC yields good psychometric data, good internal consistency (March, Parker, Sullivan, Stallings, & Conners, 1997), and is sensitive to clinical changes in anxiety related symptoms over time (March, 1997). It has demonstrated good internal consistency properties in the current sample with an alpha coefficient of .922 for the total score. Norms and clinical cut-offs for this scale are derived based on t-scores, wherein t-scores of 50 to 64 are considered in the normal to borderline range, and t-scores of 65 or greater are indicative of clinical levels of anxiety. Only the total score and corresponding t-score will be examined in this study.

Eating Disorder Inventory – 2 (EDI-2; (Garner, 1991). The EDI-2 provides a comprehensive assessment of the behavioral and psychological dimensions characteristic of EDs. The EDI-2 is a reliable and valid 91-item multidimensional self-report instrument that assesses characteristics of EDs, with higher scores indicating more severe symptomatology and/or more pathological attitudes and cognitions. The EDI-2 is divided into 11 subscales and has been found to have good psychometric properties. The specific subscales and corresponding internal consistency values (derived from an adult clinical ED sample of women aged 14 to 55 years) for those indices to be used in the current study are: Drive for Thinness (.81), Body Dissatisfaction (.91), Perfectionism (.80), Impulse Regulation (.75), Ineffectiveness (.87) and Interpersonal Distrust (.82)(Eberenz & Gleaves, 1994). These values provide evidence of good internal consistency for those subscales to be used in the current study. Possible ranges for these subscale scores are

presented in Table 1. As has been done in previous studies (Tasca et al., 2011), the additional maintenance model construct of mood intolerance will be measured using the impulse regulation subscale, the construct of core low self-esteem will be measured using the ineffectiveness subscale, and the construct of interpersonal difficulties will be measured using the interpersonal distrust subscale score.

Purging Frequency. To obtain a frequency of purging behavior for use in this study, the combination of items from two different self-report measures was employed. This is because prior to 2007, the Eating Disorder Inventory – Symptom Checklist (EDI-SC; Garner, 1991) was used to establish self-reports of ED related behaviors and symptoms. In this questionnaire, the item ‘How many times over the past month did you vomit’ was used to establish frequency over a one-month period. After 2007, self-reports of ED symptoms were established using the Eating Disorder Examination Questionnaire for Adolescents (EDEQ-A; Carter, Stewart, & Fairburn, 2001). Question 17 of the measure asks respondents to indicate the number of times the individual has vomited over the past 2 weeks for the purposes of losing weight. In order to have one measure of purging frequency, the monthly estimates from the EDI-SC were divided by two and then merged with the EDEQ-A scores to create a frequency measure of purging across a 2-week span. Although there is no evidence that supports the accuracy or validity of this method, self-report measures of frequency of symptoms are almost always retrospective and therefore considered biased, thus combining these reports in this fashion was not considered a threat to the integrity of this data.

Procedures

This study consists of secondary use of clinical data retrieved with permission from the Eating Disorder Program at CHEO. One of the clinical components of the program is the use of psychometric measures to aid in evaluating the patient's recovery over time. Batteries of clinically useful measures are administered to the patients at various intervals throughout each treatment session in order to help in understanding patients' needs. Only measures administered at the initial intake assessment and pre and post the first treatment session were used for the current study. The Research Ethics Boards at the Children's Hospital of Eastern Ontario and at the University of Ottawa approved this study.

Analytic Plan

The statistical analysis used in the current study consisted of two latent profile analyses (LPA). Latent profile analysis is a model-driven statistical approach used to identify classes of individuals who share similar combinations of behavioral profiles (B. O. Muthén, 2004). This approach uses continuous indicators to determine a categorical latent variable, and allows for the examination of unobserved subpopulations based on a combination of observed variables. A LPA has several favourable properties, namely it allows for exploratory analyses, it is flexible in that it can handle continuous and categorical data simultaneously, and also it yields a probabilistic classifying approach that allows for the assignment of group membership based on observed scores (Wang & Hanges, 2010). Additionally, this statistical technique has been shown to have a couple of advantages over standard cluster analytic techniques (e.g. k-means, fuzzy clustering) in that it has more formal criteria and fit statistics to aid in the decisions of number of

classes found (Vermunt & Magidson, 2002), and that there are relatively few assumptions needed to satisfy prior to performing this analysis (LPA can handle abnormal distributions, modest correlations between continuous indicators, missing data, etc). Prior to analysis beginning, all data were subjected to a thorough data cleaning process and missing value analysis. Data were found to be missing at random (MAR), and as LPA utilizes maximum likelihood estimation and is able to handle missing data, no missing value substitution was employed. LPA analyses were conducted using Mplus 6.2 (Muthén & Muthén, 2011).

Two LPAs were performed in order to detect whether distinct profiles of individuals based on similar behavioural profiles would emerge from data obtained at the initial intake assessment or from residual change score data derived from the first treatment encounter. The variables used in the first LPA of initial intake assessment indicators included BMI, chronicity of disorder at assessment, purging frequency, drive for thinness, body dissatisfaction, levels of depressed mood, levels of anxiety, perfectionism, interpersonal distrust, impulsivity and ineffectiveness. The variables to be used in the second LPA consist of residual change scores (Manning & Dubois, 1962) of pre to post data from across the first treatment encounter. The variables length of stay in treatment and the residual change scores for BMI, drive for thinness, body dissatisfaction, depression, anxiety, perfectionism, interpersonal distrust, impulsivity, and ineffectiveness will be included in this analysis.

Residual change scores are considered more reliable than the simple difference scores because they take into account the individuals pre-level scores when determining the amount of change that has occurred (Manning & Dubois, 1962). The residual change

score then reflects the difference between the actual observed score and the predicted value. In the current study, residual change scores of the pre to post changes across the first treatment encounter were used to explore whether progress through treatment was a good indicator of refractory status.

For the results of the LPAs, several fit indices were calculated in order to aid in determining which classification model best fits the data. No formal cut-offs exist to aid in deciding how many groups exist, instead these analyses rely on comparing indices to select the best fitting model. The Akaike Information Criterion (AIC; Akaike, 1987), the Bayesian Information Criterion (BIC; Schwarz, 1978), and the Sample-Size Adjusted Bayesian Information Criterion (SABIC; Sclove, 1987) are all goodness-of-fit indices, where lower values correspond to a better fitting model. Entropy scores are used to determine how accurate classification was performed, with higher scores indicative of greater classification accuracy. The Lo-Mendell-Rubin (LMR) adjusted likelihood test provides an inferential statistic in which it can be inferred whether the specified model fits better than a model with one less class. A significant value indicates that the number of classes specified in the particular analysis is a good fit for the data. All of these measures were used in the current study to aid in determining how many classes emerged from the two separate datasets, although the decision was based more heavily on BIC values and LMR tests, as these indices have been shown to be the most robust (Meghani, Lee, Hanlon, & Bruner, 2009; Nylund, Asparouhov, & Muthén, 2007).

Nine models were conducted for each data type, wherein different types of specifications for the covariance structure were estimated. This allowed for the modeling of different types of structures with and without freely estimated covariance structures. In

order to ascertain the most reliable model, analyses were conducted with the most restrictive model first, and then restrictions were slowly removed until the most parsimonious yet best fitting model was found (Vermunt & Magidson, 2002). As a 3-class solution was predicted, a 2-,3- and 4-class model was estimated, each with three different types of restrictions examined. Therefore, nine models in total were estimated separately for the two sets of data examined. Once the clusters were identified, class probabilities and class assignments were extracted and added to the original data file in order to examine any mean differences that existed between the groups found. After class assignment was established in the original dataset, and a series of one-way ANOVAs were performed to examine group differences amongst the emerging profiles. This method of comparison was favored over performing MANOVAs, as this type of analysis most closely resembled the mean scores obtained in the latent profile model due to missing data not limiting the estimates. Lastly, Tukey HSD post-hoc tests were performed to determine where any mean differences existed across the groups.

Results

Descriptive Statistics

The sample consisted of 324 youth who presented for an ED assessment at a local tertiary pediatric hospital, and who received intensive services due to the severity of their illness. When defining refractory disease as a return to intensive treatment, 95 (29.3%) adolescents in the sample were classified as refractory whereas 229 (70.7%) were classified as single-episode. Of the 324 adolescents who had initial intake assessment data available for analysis, only 234 had both pre and post treatment data available in order to compute the residual change score. Therefore, the second set of analysis was

performed on a subset of the original sample. Comparisons of the two adolescent subsamples reveal that the pre to post group is significantly older than the larger group, indicating that caution with the generalizability of this study findings to younger populations should be taken. Table 1 provides descriptive data for the indicator variables used in this study (at initial intake assessment only).

Initial Intake Assessment Data

The first LPA was conducted using 11 continuous indicators measured from a transdiagnostic adolescent ED group during their initial intake assessment. This allowed for the examination of how many profiles existed when refractory-related and additional maintenance variables are examined in the same classification model. As a 3-factor model was hypothesized, 2-, 3- and 4-factor models were estimated, starting with the most restrictive model followed by a model with fewer restrictions. Results of the analysis reveals that the best fitting model for the data was a 3-factor solution with class-dependent covariance values set to zero. The BIC value for this model was the lowest amongst all 9 models, and the LMR ratio test was significant ($p=.031$) indicating that the 3-class model was a better fit than the 2-class model. The entropy score was .869, suggesting high classification accuracy and good separation between class probabilities existed. Results of the goodness-of-fit indices for the nine models are presented in Table 2. According to the 3-class solution, 80 adolescents (25.2%) were classified to latent profile 1, 121 adolescents (38%) were classified to latent profile 2, and 117 adolescents (36.8%) were classified to latent profile 3. Mean differences between the three groups for almost all variables were observed. Table 3 outlines the results of the ANOVA tests.

To explore whether one of the profiles that emerged from the LPA represented a distinct refractory group, a comparison of the three profiles against refractory status, as defined by return to treatment, was performed. A chi-square analysis of the different classes that emerged from the initial intake assessment data against refractory status revealed a non-significant finding [$\chi^2(2) = .218, p = .897$], indicating that measures at initial intake assessment are not good indicators of refractory class membership.

Residual Change Score Data

Another objective of this study was to examine refractory related and maintenance variables of pre to post change scores across the first treatment encounter. This was performed to explore whether unobserved groups existed when examining progress with treatment. A LPA with 10 continuous indicators reflecting residual change scores of pre to post change across the first treatment encounter was conducted, with 2-, 3- and 4-factor models being estimated. Results of this analysis reveal that a 3-factor solution with class-dependent covariance values set to zero emerges as the superior model. Although the BIC value for this model was not the lowest amongst all 9 models, it was the model with the lowest BIC score that also had a significant LMR ratio test ($p=.021$). The entropy score for this model was moderate at .596. Table 4 displays the goodness of fit indices for the nine models. The classification results places 76 adolescent (32.5%) in latent profile 1, 60 adolescents (25.6%) in latent profile 2, and 98 adolescents (41.9%) in latent profile 3.

A comparison of the three classes that emerged from this LPA was performed in order to examine the distinct profiles, and to explore whether one class could be considered a refractory group. Results of this analysis are displayed in Table 5. The first

class that emerged from this LPA consisted of those adolescents who all achieved negative residual change on almost all refractory related and additional maintenance variables; that is, those who did better than would be predicted based on the groups' expected trajectory. Another notable characteristic of this class was that adolescents in this group on average stayed in intensive services for almost 3 months, the shortest length of stay across all three profiles. Class 2, which makes up the smallest latent profile, consists of adolescents who report the type of change that would be predicted based on the samples' mean trajectory. Adolescents in this group stayed in treatment for just under 4 months, and could be characterized as those who responded to treatment in the expected manner. The last and largest class (41.9%) contains adolescents who report positive residual change on all refractory related and additional maintenance variables, that is those who had observed scores at post that were higher than expected, indicative of poor progress while in treatment. Results of the Tukey HSD post hoc comparisons revealed significant mean differences across all indicators with regards to differences in residual change scores. Only length of stay and perfectionism were not significantly different between class 2 and class 3, otherwise all other mean differences were significantly different. Table 5 presents the results of the post hoc comparison tests.

A chi-square analysis performed with the classes that emerged from the residual change score LPA against refractory status as defined by a return to treatment revealed a significant result [$\chi^2 (2) = 16.923 p < .001$], indicating that there is significant association between the refractory status classification and the profiles that emerged from the second LPA. A crosstabulation analysis shows that adolescents who are refractory are much more likely to be classified to class 3, with 63.8% of those in this class belonging to the

refractory group. This significant finding provides some preliminary evidence that progress across the first treatment course in regards to ED related and additional maintenance factors can significantly provide a profile of a refractory course of illness. That is, those who exhibit less than expected progress within the first treatment course have close to a 64% chance of later presenting with a refractory course of illness. This significant result also demonstrated that it is progress over time and not static measures at initial assessment that better predicts profiles of refractory EDs in adolescent samples.

Comparison of classifications

A third analysis was performed to examine the relationship between those classified in the first LPA compared to those classified in the second LPA. The result of the chi-square analysis [$\chi^2(4) = 5.574, p = .233$] demonstrates a non-significant finding suggestive that the two different LPAs are not classifying the adolescents in a similar fashion. A cross-tabulation analysis of the two classification groupings further reveals that only 87 individuals were classified to the same group by both set of analysis. This analysis demonstrated that those in class 3 had the best matching rate (n=20 in class 1; n=29 in class 2; n=38 in class 3) than those in the other two classes.

Discussion

This study examined a large transdiagnostic sample of youth with EDs with the aim of determining whether distinct subgroups existed that would profile refractory cases of EDs. In this exploratory study, two different classification analyses were performed to investigate whether scores at the initial intake assessment or change scores from pre to post the first treatment encounter, produced classes of individuals that could be then be profiled to represent an adolescent refractory ED group. Several theoretically-driven ED

related refractory variables and four additional maintenance variables were modeled, with the purpose of exploring any profiles that emerged from combinations of these variables. As previous research has shown (e.g. Richard et al., 2005), much heterogeneity exists with regards to our understanding of refractory status in the EDs. Thus, this study aimed to characterize this heterogeneity by studying whether unobserved groupings derived from several observed indicator variables of refractory status can enhance our current understanding.

Patient-level characteristics captured at the initial intake assessment have been shown to have predictive ability of those who may be at risk of a refractory ED (e.g. Castro et al., 2004). Thus, a classification analysis of these indices to see whether there is a specific profile that exists among these indicators was performed. The results of the LPA revealed a 3-factor structure that best fits the data, which is consistent with the number, but not the type of groups hypothesized in this study. The high entropy score that was obtained (.869) provides an indication that this model was highly accurate at classifying these adolescents into the emerging groups. This confirms that three groups exist when examining refractory related and additional maintenance variables assessed at initial intake assessment in clinical samples of youth with EDs. Based on analyses exploring differences between profiles, non-significant results were yielded, indicating that profiles that exist based on characteristics at initial intake assessment do not differentiate a refractory group as operationalized in this study. It may be the case that initial intake characteristics are not sensitive enough to define refractory EDs, or that this course of illness is not detectable or present until later on in treatment or developmental age.

As some evidence exists that posits that change while in treatment is predictive of refractory status (e.g. McFarlane et al., 2008), a second LPA was performed to examine whether progress over the course of the first intensive treatment round helped to identify refractory cases. Similar to the number of profiles that emerged from the initial intake analysis, findings of the second LPA on change in the first treatment course revealed a 3-class solution that best fits the data. This suggests that when examining refractory related and additional maintenance variables either at initial intake or across the first treatment encounter, three types of profiles exist.

The three profiles that emerged had some interesting properties. The first profile contained adolescents whose mean scores on all post measures were better than would be predicted based on the samples average progress trajectory, indicating that this group responded to treatment more favourably than would be expected. This class also had the shortest length of stay of all three groups, which corresponds to the positive change observed in pre and post treatment scores. The second group that emerged contained adolescents who responded to treatment as would be predicted based on the samples mean progress scores. Across almost all indicators, very small residual change scores were observed, which corresponds to those who generally did as expected with treatment. Class 3 contained adolescents who had large positive residual changes across their pre to post scores. This is indicative of ED related and additional maintenance factors that did not improve as expected with treatment. Based on the residual scores obtained, it could be possible that many of those who were classified to profile 3 would be those individuals who may require further intensive services, due to the lack of change or worsening of symptoms that occurred across the first treatment encounter. The post hoc tests performed

with these classes suggests that many of the indices differed significantly across all groups, with the exception of perfectionism and length of stay between class 2 and class 3, and BMI scores between class 1 and 3. These comparisons do not necessarily provide a clearer picture as to whether one of the groups could be labeled more definitively as a refractory group, but do provide evidence that significant differences exist amongst the groups based on their trajectories across the first treatment encounter.

Evidence that three groups or classes exist in this adolescent sample when examining refractory related and additional maintenance variables across the first treatment encounter was found. A comparison of the classification results against refractory status as defined by a return to treatment revealed a significant finding, suggestive that these groups do resemble one another. A closer look at this finding demonstrated that the third profile contained the majority of those who were classified as refractory. These results suggest that change score indicators across the first treatment course are better at identifying those who may present with a refractory ED, versus data gathered at the initial intake assessment. Therefore clinicians and treating professionals should pay more attention to progress indicators than to initial assessment characteristics when trying to establish refractory EDs. This provides one of the first accounts as to which type of data is better identifying a refractory ED, and suggests that adolescents' progress over the course of treatment provides a more accurate prediction as to whether one might suffer from a refractory ED than does characteristics at initial assessment. That is, those adolescents who display less than expected progress across treatment should be monitored closely for risk of a refractory course.

Although some recent evidence exists (e.g. McFarlane et al., 2008) that has started to explore the predictability of progress indicators at detecting a refractory course of illness, to date there are no adolescent studies of this kind, nor any studying a transdiagnostic sample. Even though previous studies have found that response to treatment, higher BMI at discharge, and residual ED symptoms have been significantly linked to the prediction of relapses in adults (McFarlane et al., 2008), no similar studies to date have looked at the additional maintenance factors in combination with other ED related variables, and explored whether profiles exist that better predict refractory EDs in adolescents. The current study provided one of the first accounts of those progress indicators that may help identify refractory courses of illness. Also, as it was shown that it was profiles of the progress indicators and not profiles from initial intake that are more predictive of an adolescent with a refractory ED, clinicians should focus more on how an adolescent progresses over treatment as an indicator of whether a refractory course of illness is present.

Although the hypothesized subgroups did not emerge based on the indicators investigated in this study, three profiles were found to exist amongst youth with EDs with regards to ED related and additional maintenance factors. Also interesting is that three distinct profiles existed regardless of whether examining initial assessment data or change score data across the first treatment encounter. These findings suggest that regardless of data type, the combination of ED related and additional maintenance indicators resulted in three different types of adolescent ED profiles. This finding alone is worthy of further investigation to explore whether diagnostic classifications may aid in better defining

these groups, or to explore whether other prognostic indicators might be more helpful in distinguishing between these three groups.

Limitations

This study was limited in that it was exploratory in nature, and therefore cannot yet be generalized to other samples until further testing in different samples has revealed similar findings. Also, as this study presents as one of the first investigations of this type, only those variables that were theoretically applicable were included, limiting our understanding as to whether other variables may have added significantly to the profiles of those with a refractory ED. Future studies should aim to investigate different types of factors or indicators in order to gain a full picture of these youth.

Other limitations of this work are the sole use of self-report measures to examine these profiles. Although this limits the interpretation to only those answers that were provided by the youth, future studies should strive to examine parent and/or clinician measures in order to corroborate the findings. Furthermore, Fairburn and colleagues maintenance model (2003) includes core eating disorder variables, described as eating concern, shape concern and weight concern. Although this study was not able to include these variables due to a lack of a developmentally appropriate measure (i.e. the Eating Disorder Examination Questionnaire), future studies should aim to include all variables pertinent to the maintenance model in order to best understand how this theory relates to refractory ED cases in youth.

Future Directions

Future work in this area should attempt to replicate these findings in similar clinical samples of youth with EDs. In addition, replicating these findings in adult

samples would also provide further evidence that profiles based on refractory related variables coupled with reports of the additional maintenance variables could reliably identify profiles of adolescents at risk of facing a refractory course of illness. Future studies should also investigate the influence of diagnosis on the classification of these profiles, and should potentially also examine the effect of age, presence of family history of EDs and alcohol abuse (Steinhausen et al., 2008), as these variables have all had some relation to refractory EDs in past studies. Further, results of the second LPA performed with residual change scores demonstrates the emergence of three distinct trajectories; that is; adolescents who do better than expected, adolescents who respond to treatment as expected, and adolescent who do worse than expected with treatment. This suggests that three distinct trajectories exists, therefore future studies should examine longitudinal data in order to understand and study these trajectories in greater detail. Lastly, and with respect to evaluating change scores for the purpose of finding profiles, the inclusion and study of graduation status (completer, partial completer, drop-out) could also lend to more accurate classification results.

This exploratory study examined refractory related and additional maintenance profiles of youth with EDs who underwent intensive treatment for their moderate to severe ED. Results revealed distinct classes of adolescents that emerge, with data from both the initial assessment and change scores across the first treatment encounter reliably separating three different profiles. This leads to the conclusion that three distinguishable profiles exist when studying measures theoretically related to refractory EDs in adolescent samples, regardless of whether at initial assessment or based on progress across treatment. In addition, another major finding of this study is that progress

indicators, and not initial intake data, provide significant information regarding whether an individual is at risk of developing a refractory ED. This suggests that future research should continue to investigate the predictability of progress indicators in detecting refractory EDs. From a clinical standpoint, these findings suggest the need for, and monitoring of, pre and post levels of those factors found to be related to refractory EDs, as those individuals with less progress than would be expected are more likely to be at risk of requiring a return to treatment. Close monitoring and continued work on ED related and additional maintenance factors related to refractory EDs could aid in preventing a refractory course, or potentially lessen the number of treatment courses needed.

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Table 1. Descriptives of ED related and additional maintenance predictors (n=324).

INDICATOR	Mean	<i>SD</i>	Reported Range	Possible Range
INTAKE ASSESSMENT SCORES				
Body Mass Index (kg/m ²)	17.89	2.98	12.40 – 28.00	--
Drive for Thinness	13.16	7.44	0 – 21	0 – 21
Body Dissatisfaction	15.23	9.54	0 – 27	0 – 27
Depressed Mood (t-score)	66.31	18.16	34 – 100	34 – 100
Anxiety (t-score)	59.27	12.27	25 – 90	25 – 100
Perfectionism	7.03	4.73	0 – 18	0 – 18
Interpersonal Distrust	5.43	4.63	0 – 18	0 – 18
Impulsivity	6.41	6.53	0 – 27	0 – 27
Ineffectiveness	10.86	8.84	0 – 29	0 – 30
Chronicity (months)	16.95	13.99	0 – 66	--
Purging frequency (over 2 weeks)	11.80	11.49	1 – 45	--
Length of Stay (days)	109.90	57.47	6.00 – 273.00	--

Table 2. Results of latent profile analysis of initial intake assessment data (n=324)

	Likelihood	AIC	BIC	SABIC	Entr opy	LMR Ratio Test	
						-2LL	<i>p</i>
Cluster = 2							
Class-ind. unrestricted Σ_k	-8572.70	17323.41	17658.23	17375.94	.855	154.89	.000
Class-dep. diagonal Σ_k	-8712.08	17514.16	17683.45	17540.73	.897	1323.75	.001
Class-ind. diagonal Σ_k	-8854.02	17776.04	17903.95	17796.11	.871	1039.86	.000
Cluster = 3							
Class-ind. unrestricted Σ_k	-8523.94	17249.88	17629.85	17309.50	.825	97.53	.051
Class-dep. diagonal Σ_k	-8452.71	17041.44	17297.25	17081.56	.869	518.73	.031
Class-ind. diagonal Σ_k	-8673.52	17439.04	17612.10	17466.20	.856	361.00	.001
Cluster = 4							
Class-ind. unrestricted Σ_k	-8488.46	17202.92	17628.03	17269.62	.835	74.83	.703
Class-dep. diagonal Σ_k	-8386.66	16955.33	17297.67	17009.04	.819	132.10	.269
Class-ind. diagonal Σ_k	-8622.63	17361.26	17579.45	17395.49	.855	101.79	.406

Table 3. Means, standard errors, and ANOVA results for the latent class indicators measured at initial intake assessment

Indicators	Class 1 (n=80)	Class 2 (n=121)	Class 3 (n=117)	<i>F</i> (<i>p</i> -value)
Body Mass Index (kg/m ²) ^{bc}	16.41 (.264)	17.05 (.282)	19.93 (.393)	44.58 (.000)
Chronicity (in months) ^{bc}	9.02 (.714)	13.42 (1.366)	26.64 (2.649)	28.51 (.000)
Purging frequency (2 wks)	3.25 (.895)	9.35 (1.870)	13.82 (1.629)	2.74 (<i>ns</i>)
Drive for Thinness ^{abc}	2.78 (1.386)	13.67 (.749)	18.76 (.309)	283.64 (.000)
Body Dissatisfaction ^{abc}	3.50 (.829)	13.35 (1.110)	23.67 (.608)	279.52 (.000)
Depressed Mood (t-score) ^{abc}	45.65 (1.732)	61.78 (1.878)	89.74 (1.269)	338.70 (.000)
Anxiety (t-score) ^{abc}	48.08 (.081)	59.67 (1.232)	66.35 (1.080)	76.72 (.000)
Perfectionism ^{abc}	4.33 (.732)	6.64 (.473)	8.95 (.450)	24.89 (.000)
Interpersonal Distrust ^{abc}	1.21 (.241)	5.17 (.556)	8.14 (.445)	66.05 (.000)
Impulsivity ^{abc}	.60 (.150)	4.29 (.680)	11.78 (.676)	135.45 (.000)
Ineffectiveness ^{abc}	1.06 (.303)	7.64 (1.000)	19.50 (.723)	361.29 (.000)

^a Significant difference between Class 1 and Class 2

^b Significant difference between Class 1 and Class 3

^c Significant difference between Class 2 and Class 3

Table 4. Results of Latent Profile Analysis with Residual Change Scores (n=234)

	Likelihood	AIC	BIC	SABIC	Entr opy	LMR Ratio Test	
						-2LL	<i>p</i>
Cluster = 2							
Class-ind. unrestricted Σ_k	-4393.58	8939.17	9201.77	8960.89	.589	45.81	.372
Class-dep. diagonal Σ_k	-4507.60	9097.19	9238.86	9108.91	.626	408.16	.355
Class-ind. diagonal Σ_k	-4527.04	9116.08	9223.20	9124.94	.600	369.27	.000
Cluster = 3							
Class-ind. unrestricted Σ_k	-4371.75	8917.50	9218.12	8942.37	.572	34.63	.536
Class-dep. diagonal Σ_k	-4440.83	9005.67	9219.90	9023.39	.596	133.53	.021
Class-ind. diagonal Σ_k	-4483.60	9051.19	9196.32	9063.19	.571	86.89	.293
Cluster = 4							
Class-ind. unrestricted Σ_k	-4355.26	8906.53	9245.15	8934.53	.678	29.46	.732
Class-dep. diagonal Σ_k	-4402.35	8970.69	9257.49	8994.41	.635	76.97	.349
Class-ind. diagonal Σ_k	-4451.64	9009.28	9192.41	9024.43	.640	63.91	1.00

Table 5. Means, standard errors, and ANOVA results for the residual change scores across the first treatment encounter

Indicators	Class 1 (n=76)	Class 2 (n=60)	Class 3 (n=98)	<i>F</i> (<i>p</i> -value)
Body Mass Index (kg/m ²) ^{ac}	-.54 (.597)	1.23 (.684)	-.64 (.528)	12.32 (.000)
Length of Stay (days) ^{ab}	86.84 (7.818)	113.50 (10.123)	122.87 (8.211)	28.19 (.000)
Drive for Thinness ^{abc}	-6.88 (.749)	-2.15 (.763)	6.11 (.687)	95.41 (.000)
Body Dissatisfaction ^{abc}	-10.62 (.668)	-3.25 (1.172)	9.19 (.553)	196.32 (.000)
Depressed Mood ^{abc}	-13.94 (1.197)	-2.47 (1.460)	11.84 (1.490)	129.58 (.000)
Anxiety ^{abc}	-7.80 (1.409)	-.51 (1.279)	5.67 (1.198)	37.45 (.000)
Perfectionism ^{ab}	-2.96 (.432)	.67 (.596)	1.34 (.467)	20.74 (.000)
Interpersonal Distrust ^{abc}	-2.41 (.298)	-.12 (.525)	1.68 (.408)	22.57 (.000)
Impulsivity ^{abc}	-3.01 (.493)	-.14 (.747)	2.01 (.594)	17.11 (.000)
Ineffectiveness ^{abc}	-6.60 (.631)	-2.44 (.550)	6.25 (.916)	105.67 (.000)

^a Significant difference between Class 1 and Class 2

^b Significant difference between Class 1 and Class 3

^c Significant difference between Class 2 and Class 3

**Growth Trajectories of Maintenance Variables Related to
Refractory Eating Disorders in Youth**

Abstract

Eating disorders (EDs) rank as the third most common chronic illness among adolescent females, and high rates of relapse and chronicity are often seen. In spite of decades of ED research, longitudinal studies of factors involved in refractory EDs, defined as requiring a return to same-type treatment, are still lacking. The objective of the current study was to investigate longitudinally, the role of the additional maintenance variables found in Fairburn et al's., model (2003) for their role in refractory EDs. Participants in this study consisted of 305 adolescents with a moderate to severe ED, who underwent intensive specialized treatment. Growth trajectories of data collected during the initial intake assessment, at pre and post treatment and at 6 month and 1 year follow-ups were explored. A confirmatory factor analysis (CFA) was performed in order to investigate whether the four additional maintenance factors could be joined to create a summary maintenance factor, and hierarchical linear modeling (HLM) was used to explore growth trajectories of this summary factor. The results of the CFA demonstrated that the four additional maintenance factors do share similar properties, and therefore all load well onto a common summary maintenance factor. Results of the HLM revealed that a significant cubic growth pattern exists when examining the summary maintenance factor over time, wherein there is a slight increase in symptoms while waiting for treatment to begin, then a decline in symptoms with treatment, followed by a slight rebound of symptoms during follow-up. This suggests that the intensive specialized ED treatments are successful at decreasing those factors thought to be involved in maintaining an ED by post treatment, although the lasting benefits of this treatment is still not clear. Further clinical implications of these findings are discussed.

Growth Trajectories of Maintenance Variables Related to Refractory Eating Disorders in Youth

Eating disorders (EDs) rank as the third most common chronic illness among adolescent females (Fisher et al., 1995), with reports indicating a 25-year reduction in lifespan when the age of onset occurs between 10 to 15 years of age (Norris, Bondy, & Pinhas, 2011). Eating disorders also have one of the highest rates of medical complications among any of the psychiatric disorders (Mitchell & Crow, 2006), and are frequently associated with greater psychological comorbidities and severe life impairment (Ackard, Fulkerson, & Neumark-Sztainer, 2011; Godart, Flament, Perdereau, & Jeammet, 2002; Hudson, Hiripi, Pope, & Kessler, 2007). Also concerning is the ‘unusual tenacity’ of these disorders (Strober et al., 1997), and the high rates of relapse and chronicity often seen with EDs (Richard, Bauer, & Kordy, 2005).

Current trends of long-term ED outcome studies reveal a poor prognosis. In the adult ED literature, published relapse rates vary from 30% (Olmsted, Kaplan, & Rockert, 2005) to 63% (Field et al., 1997), and 10-year follow-up review studies of anorexia nervosa (AN) report that only 57.1% make a full recovery, 25.9% have residual symptoms, 16.9% remained severely ill and chronic, and 1.8% died of AN-related causes after 10 years (Steinhausen, 2002). The prognosis for those with bulimia nervosa (BN) presents with a similar picture, with estimates of 21% to 75% attaining remission (Ben-Tovim et al., 2001; Grilo et al., 2003; Herzog et al., 1999; Keel et al., 2004, 2005), and review studies of long-term follow-ups revealing recovery rates of just over 50% after 5 to 10 years (P. Keel & Mitchell, 1997). The large discrepancies found in these studies have been attributed to the differing operational definitions of recovery or relapse, the

varying follow-up periods studied spanning from 12 months to 15 years (e.g. Salbach-Andrae et al., 2009; Strober et al., 1997), the small clinical sample sizes, and the diagnostic and sampling heterogeneity of the studied samples (Holle et al., 2008). A consequence of this inconsistency is that a reliable account of relapse and recovery in EDs remains unclear.

In spite of decades of ED research, identifying those individuals who might be at risk of poor long-term outcomes is still under debate. This may be because a clear definition of relapse and recovery, as it applies to the EDs, is still not agreed upon across clinicians and researchers (Quadflieg & Fichter, 2003; Steinhausen, 2002; Walsh, 2008). Although recovery, relapse, and long-term outcomes all vary in definition and operationalization across the ED literature, what is certain is that those who return for a second or third course of the same type of treatment represent those individuals who have experienced a true relapse. Thus, those individuals who require a return to treatment could be conceptualized as having a refractory course of illness. The term refractory in medical terminology refers to those individuals whose illness is resistant to treatment (US National Library of Medicine, 2012), which coincides with the proposed definition.

Limited research on refractory EDs has been conducted in adolescent populations, even though it is well documented that EDs have their onset in adolescence (Bryant-Waugh, 2006; Lock & Gowers, 2005). Even more scarce are the number of adolescent studies that have examined ED trajectories over time, leading to a dearth of understanding as to the mechanisms of change in ED symptoms and their persistence. The need for longitudinal studies in clinical samples of adolescents that examine ED

related factors over time and treatment are essential to explore what maintains this disorder.

Relatively few theories have been proposed to explain what maintains an ED. Fairburn and colleagues' (Fairburn et al., 1986) cognitive-behavioural model for bulimia nervosa is among the first eating pathology maintenance model that has been proposed and empirically tested (Byrne & Mclean, 2002). This model posits that dietary restraint, eating, weight and shape over-concern and evaluation is the primary maintaining factor in binge eating. The model further contends that the binge eating in turn leads to the use of extreme compensatory behaviours in pursuit of the thin ideal. In this fashion, dieting is conceptualized as a mediator between appearance over-evaluation and bulimic symptoms, providing a maintenance factor to the disordered eating.

The term maintenance factor is often cited in this literature as those variables thought to maintain the disease state. Stice (2002) defined maintenance factors as those that predict symptom persistence versus symptom remission. In his review of risk and maintenance factors involved in eating pathology (Stice, 2002) he found support for four maintenance factors of eating pathology: a) thin ideal internalization, b) body dissatisfaction, c) negative affect, and d) perfectionism.

In 2003, developers of the cognitive behavioral-maintenance model for BN refined their model to allow it be transdiagnostic, and to include four additional maintenance factors (Fairburn, Cooper, et al., 2003). According to their new transdiagnostic theory of the maintenance of EDs, certain individuals with EDs will have one or more of the four additional maintenance factors interact with the original three core eating disorder pathology factors (over-evaluation of eating, shape and weight and

their control) and this acts as an obstacle to change. The four additional maintenance factors that these authors propose are: core low self-esteem, interpersonal difficulties, perfectionism, and mood intolerance. They argue that the model should apply to all three major categories of EDs (AN , BN and EDNOS), as these ED categories are theorized to share the same distinctive psychopathology, and evidence suggests that patients migrate between these diagnostic states over time (Tozzi et al., 2005). Empirical support for this model as a transdiagnostic theory is beginning to emerge in adult samples (e.g. Tasca et al., 2011). Similarly, support for this model in younger age groups has also emerged, with a recent study investigating this model in an adolescent community sample of binge eating disorder (Allen, Byrne, & McLean, 2012). Research examining this theory and the applicability of the additional maintenance factors in a clinical transdiagnostic sample of adolescents with EDs is still non-existent, despite the need to better understand this ED trajectory in clinical samples of youth.

An examination of the properties of the transdiagnostic model over time may provide a more accurate account of how these factors operate to maintain the ED. Although some studies have emerged that examine the maintenance factors involved in refractory EDs, they are limited to cross-sectional designs (e.g. Lampard et al., 2011). Examining this model in adolescence using a longitudinal developmental approach could contribute much needed knowledge to the field. Therefore, a longitudinal growth curve study of adolescent EDs that examines change in the maintenance factors postulated to play a role in refractory EDs is proposed for the current study, as such research is strongly needed to help support this model and understand the developmental nature of how these factors are changing and influencing the course of an ED in adolescents.

To date, there are no studies that have examined the growth trajectories of adolescent EDs relating to maintenance factors. There is also a paucity of studies that have examined maintenance factors related to refractory EDs using longitudinal data. The lack of studies that examine individual change in these factors has limited the identification of factors involved in refractory EDs, and impedes the development of more tailored treatment programs aimed at reducing the incidence of a refractory ED. Exploring maintenance factors, refractory course of illness, and growth trajectories of illness in adolescents will allow for better identification of patients at risk for a refractory course.

The aim of the current study was to explore the growth trajectories of the four additional maintenance variables across five time points in a clinical sample of adolescents with EDs. The five time points to be examined include the initial intake assessment, pre and post first treatment course measurement, and 6 months and 1-year follow-ups. This study will provide one of the first examinations of ED maintenance profiles over the course of multiple time points for adolescents who receive intensive treatment for a moderate to severe ED.

The first objective of this study is to examine whether the four additional maintenance variables can be combined to create a summary maintenance factor. A confirmatory factor analysis (CFA) will assess whether this measurement model provides a good fit, and whether the four scores reliably and validly measure a maintenance summary score. As previous studies have confirmed a significant measurement model amongst the additional maintenance variables in adult samples

(Tasca et al., 2011), it is likely that these factors will share similar properties in an adolescent sample.

The second objective of this study was to explore the growth trajectories of the summary maintenance factor in a longitudinal fashion. As no evidence exists that has explored the phenomenon of maintenance factors over time in a large clinical sample of youth with moderate to severe EDs, a clear hypothesis of the relationship between the variables and the shape of the trajectories was not possible. With evidence showing that many psychological symptoms are relieved with intensive ED treatment (e.g. Lock et al., 2010; le Grange, Crosby, Rathouz, & Leventhal, 2007), and that there is usually a slight rebound of symptoms once intensive treatment has terminated (Lowe, Davis, Annunziato, & Lucks, 2003), it was hypothesized that a non-linear growth pattern would exist. More specifically, a quadratic or cubic type growth pattern is predicted, wherein there may or may not be an increase in maintenance symptoms while waiting for treatment to initiate, which would subsequently be followed by a decrease in symptoms while involved in intensive treatment, which would then be followed by a possible increase in symptoms once the individual has left the therapeutic environment.

The third objective was to examine whether variability exists in the growth curves, and if present, whether the addition of a between-person predictor helped explain some of the variability in the maintenance scores. The person-level predictor that was explored in the current study was refractory status, defined by a return to same-type treatment. It was hypothesized that this predictor would partially explain some of the variability found in the summary maintenance score across individuals.

Methods

Participants

The sample consisted of 305 ED patients who received specialized inpatient and/or day hospital treatment between January 2000 and January 2011 from a tertiary care hospital located in Ottawa, Canada. Mean age of the sample was 15.23 years ($SD=1.77$), and ranged from 8.52 to 17.92 years of age. There were 289 females (94.8%) and 16 males (5.2%). Data retained for use in this study consisted of participants' self-report measures collected at the initial intake assessment, pre and post-treatment across the first treatment course, and at 6-month and 1-year follow-up from initial intake assessment. Participants were excluded from analysis if they received outpatient care exclusively, or if their follow-up measurements occurred before treatment was initiated (i.e. those patients who did not require intensive treatment until 1 year after initial assessment).

Description of Eating disorder program

Participants of this study consisted of individuals who were treated by the regional ED program located at the Children's Hospital of Eastern Ontario. The population treated includes children and adolescents aged 8 to 18 years from across the province, serving a population of approximately 1.5 million. Patients are referred through three channels, either via their family physician, the local emergency department, or through a provincial network. Two specialized group-based intensive programs are offered: Inpatient or Day Hospital services. Both programs are group-based integrated programs primarily based on Maudsley family-based treatment (FBT) principles (Lock & Fitzpatrick, 2007), wherein the parents are empowered to support their child in recovery.

The program also incorporates some components of cognitive-behavioural treatment, dialectical behaviour therapy, mindfulness, expressive arts therapy, pet therapy and interpersonal therapy.

Day Hospital Program. The Day Hospital Eating Disorder Program has been in operation since 2000, and represents the first specialized partial hospitalization treatment program offered in the region. The program has a maximum capacity of 8 youth, and operates from 8am to 6pm 5 days per week. The typical length of program is 12-14 weeks, and approximately 35 patients are treated each year. During the course of the program, all recipients receive group therapy, meal support, academic support, therapeutic outings, and individual and family therapy. This program is often used as a step-down treatment plan for those who successfully complete the inpatient program.

Inpatient Program. Since the formal opening of the program in January of 2007, the Inpatient Eating Disorder program has treated approximately 45 to 55 children and youth each year, with average lengths of stay ranging from 30 to 60 days. This group-based treatment program has six inpatient beds, allocated on a shared child psychiatric ward of a local tertiary care pediatric hospital. The main goal of the specialized inpatient program is medical stabilization, although normalization of eating, nutritional rehabilitation, and reduction of comorbid symptoms is also a focus. Individual and FBT are also essential to the inpatient program.

Maudsley principles of empowering parents to support their child in recovery (Lock & Fitzpatrick, 2007).

Assessment Measures

Demographic data. The demographic variables age, gender, BMI, diagnosis, treatment modality, and chronicity of illness at assessment were collected from clinical charts. These data were employed mostly for descriptive purposes.

Eating Disorder Inventory – 2 (EDI-2; Garner, 1991). The EDI-2 provides a comprehensive assessment of the behavioral and psychological dimensions characteristic of EDs. The EDI-2 is a reliable and valid 91-item multidimensional self-report instrument that assesses characteristics of EDs, with higher scores indicating more severe symptomatology and/or more pathological attitudes and cognitions. The EDI-2 is divided into 11 subscales and has been found to have good psychometric properties. The specific subscales and corresponding internal consistency values (derived from an adult clinical ED sample of women aged 14 to 55 years) for those indices to be used in the current study are: Drive for Thinness (.81), Body Dissatisfaction (.91), Perfectionism (.80), Impulse Regulation (.75), Ineffectiveness (.87) and Interpersonal Distrust (.82)(Eberenz & Gleaves, 1994). These values provide evidence of good internal consistency for those subscales to be used in the current study. Possible ranges for these subscale scores are presented in Table 1. As has been done in previous studies (Tasca et al., 2011), the additional maintenance model constructs of mood intolerance will be measured using the impulse regulation subscale, the construct of core low self-esteem will be measured using the ineffectiveness subscale, and the construct of interpersonal difficulties will be measured using the interpersonal distrust subscale score.

Procedures

This study consists of secondary use of clinical data retrieved with permission from the CHEO Eating Disorder Program. One of the clinical components of the program surrounds the use of psychometric measures to aid in evaluating the patient's recovery over time, thus a battery of clinically useful measures were administered to the patients at various intervals throughout treatment in order to help in understanding the patients needs. Measures used in the current study were collected at the initial intake assessment, pre and post the first treatment encounter, and at 6 months and 1-year follow-up. The Research Ethics Boards at the Children's Hospital of Eastern Ontario and at the University of Ottawa approved this study.

Analytic Plan

The first objective of this study was to determine whether the four additional maintenance variables described in Fairburn et al.'s model (2003) could be combined to create a summary maintenance factor that could then be modeled over time. A confirmatory factor analysis (CFA) using the Analysis of Moment Structures program (AMOS; Arbuckle, 2003) version 19 was used to test the measurement model. The criteria used to assess model fit were the comparative fit index (CFI) and root mean square error of approximation estimates. These criteria were used as they are least affected by sample size (Fan, Thompson, & Wang, 1999), and have been deemed the most useful measures of model fit (Thompson, 2000). A CFI estimate of .95 or greater, and a RMSEA estimate of less than or equal to .05 are considered good model fit (Hu & Bentler, 1999; Schumacker & Lomax, 2004).

The second aim of the current study was to examine change over time, or growth trajectories, of the summary maintenance variable, and to explore whether certain predictors helped explain any inter-individual variability that exists in the growth patterns. In order to pursue this goal, hierarchical linear modeling (HLM) was employed using HLM7 software (Raudenbush, Bryk, & Congdon, 2010). This type of analysis is best conceptualized as a two level type of analysis (Bryk & Raudenbush, 1987; Singer & Willett, 2003). In the first stage, the level 1 model examines person-specific growth rates and is commonly referred to as the within-person or intra-individual change model. The second stage of the model, or the level 2 model, is commonly referred to as the inter-individual change model, as it captures between-person variability in the growth rates. That is, once it is established that variability exists in the growth curves, predictors can be added to the model to try to estimate those characteristics that help explain the variability. Specifically, time-invariant predictors (e.g., gender, ethnicity) can be included at level 2, to try to explain the variability in the growth curves, whereas time-variant predictors are usually added to the Level 1 model. Another important benefit of HLM is that it has tremendous flexibility when it comes to missing data. This type of analysis can easily incorporate all individuals who have at least one time point, as long as the missing data is missing at random (Raudenbush & Bryk, 2002), as is the case in the current dataset.

In the current study, several growth models were explored at Level 1 as it was hypothesized that a non-linear growth pattern existed across the 5 time points. To find the best fitting and most parsimonious model, first a linear model was explored, followed by a model with linear and quadratic growth terms, and then a model with linear, quadratic and cubic terms. Differences between deviance scores derived using full maximum

likelihood were then computed in an attempt to isolate the best-fitting model. The following models were examined, with all Time terms centered at the post treatment score (midpoint).

$$\text{Level 1: Maintenance} = \pi_0 + \pi_1(\text{TIME}) + \pi_2(\text{TIME}^2) + \pi_3(\text{TIME}^3) + e$$

$$\text{Level 2: } \pi_0 = \beta_{00} + r_0$$

$$\pi_1 = \beta_{10} + r_1$$

$$\pi_2 = \beta_{20} + r_2$$

$$\pi_3 = \beta_{30} + r_3$$

Further, a dichotomous time-invariant predictor, refractory status (0=single-episode, 1=refractory), was added as a level 2 predictor, to study whether it helped explain some of the variability in the individual growth curves. The following model that includes the level 2 predictor was tested:

$$\text{Level 1: Maintenance} = \pi_0 + \pi_1(\text{TIME}) + \pi_2(\text{TIME}^2) + \pi_3(\text{TIME}^3) + e$$

$$\text{Level 2: } \pi_0 = \beta_{00} + \beta_{01}(\text{Refractory Status}) + r_0$$

$$\pi_1 = \beta_{10} + \beta_{11}(\text{Refractory Status}) + r_1$$

$$\pi_2 = \beta_{20} + \beta_{21}(\text{Refractory Status}) + r_2$$

$$\pi_3 = \beta_{30} + \beta_{31}(\text{Refractory Status}) + r_3$$

Centering of the time variable was created at the middle point, as it has been shown that mid-point centering is desirable when examining higher-order polynomials in growth curves. As Raudenbush and Bryk (2002) point out, centering in the middle will define the linear slope as the ‘average velocity’ during the data collection period specified (i.e. not at the initial onset), and it also minimizes the correlation between the time parameters with the desired effect of stabilizing the estimation procedure. Therefore in the current

study, the time points were centered at time point 3 or at post-treatment. Using this centering point, the linear model then studied whether a straight line best explained the maintenance trajectory across the five timepoints. The quadratic model explored whether a decrease in maintenance scores is expected at post treatment followed by an increase in maintenance factors during the follow-up periods. The cubic model studied whether there was an initial increase in the summary maintenance factor between initial assessment and the commencement of treatment, which was followed by a decrease pre to post treatment, and then an increase in symptoms again during follow-up.

Results

Descriptive Statistics

Data from a total of 305 youth who presented for an ED assessment at a local tertiary pediatric hospital and who received intensive services were included in this study. Of the original 324 participants who were eligible for this study, 19 were excluded on the basis that their 6-month follow-up occurred prior to their pre and or post treatment data points. Based on a consensus diagnosis, 156 (51.1%) youth were diagnosed with AN, 35 (11.5%) were diagnosed with BN, and 114 (37.4%) were diagnosed with EDNOS. When defining refractory disease as a return to intensive treatment, 86 (28.2%) adolescents in the sample are classified to the refractory group and 219 (71.8%) are classified to the single-episode group. Descriptive details of the indicator variables at all 5 timepoints are provided in Table 1. Before analyses were conducted, the data were subjected to a missing value analysis, which showed that missing data in this sample were missing at random (Little, 2005).

Confirmatory Factor Analysis of Summary Maintenance Variable

A confirmatory factor analysis was performed in order to test whether the four additional maintenance variables could be combined to create a summary maintenance factor. The variables perfectionism, interpersonal distrust, impulse regulation and ineffectiveness were placed into a measurement model in AMOS and were tested for their model fit. Figure 1 depicts the model that was tested.

The results of the analysis reveal an excellent model fit, with $\chi^2(2)=1.506$, $p=.471$, and CFI = 1.000 and RMSEA = .000 (90% CI: .000 to .101). The results of this CFA demonstrate that the four additional maintenance variables do indeed load adequately onto one overarching factor, and therefore a summary maintenance variable is warranted. Given the good model fit and that all four subscales are derived from the same instrument, the summary maintenance factor for each timepoint was thus defined as the weighted mean of perfectionism, interpersonal distrust, impulse regulation and ineffectiveness. To create this factor score, each indicator was multiplied by its respective factor loading prior to being calculated as a mean, in order to take into account the weighting of each indicator.

Growth Curve Trajectories

The second objective of the current study was to explore the growth trajectories of the summary maintenance factor in a large transdiagnostic sample of youth with EDs. This includes identification of the correct form of growth (e.g., linear, quadratic, or cubic), as well as specification of the variance of the individual growth estimates (e.g., intercept and slope). A graph of the mean levels of the summary maintenance factor across all five time points suggests a cubic growth curve pattern exists (see Figure 2).

According to the graph, average levels of the summary maintenance factor initially increased just slightly between the initial intake assessment and pre-treatment, then decreased during treatment, and then increased again during follow-up. The difference test of the deviance statistics between the linear and quadratic model was significant [$\chi^2(4) = 7.907, p < .001$] indicating that the quadratic model was a better fit than the linear model. The difference test between the cubic and quadratic model was significant [$\chi^2(5) = 144.353, p < .001$] suggesting that a cubic growth curve better models the summary maintenance factor trajectory than a quadratic curve.

Several growth parameters were estimated for the summary maintenance variable, where first a linear model was fit, then a linear and quadratic model were tested, and lastly a linear, quadratic and cubic model were fit. Results of the analysis show that all but the quadratic term emerged as a significant growth pattern (see Table 2). That is, significant linear and cubic growth patterns were found, and although the linear model would be more parsimonious, the significant cubic growth pattern suggests that this type of model better fits the data. Table 2 provides the estimates of the growth curve. The results of this analysis reveal that there was a significant linear trend across the five timepoints, and the sign of the coefficient signals a decreasing linear trend from initial intake to 1 year follow-up. There was also a significant cubic pattern that emerged, which revealed an s-shaped pattern of growth across all 5 timepoints. This pattern of change was one where it first increased (intake to pre), then decreased (pre to post), then subsequently increased again (post to follow ups). The cubic variance component was significant in this model, indicating that these curves vary across all individuals in the

sample. This significant variance term also suggests that between-person (level 2) predictors could be added to the model to try to explain this variability.

Refractory Status as a Predictor of Variability in Growth Curves

As viewed in Table 3, refractory status only significantly predicted the variability in the intercept and linear relationship ($p < .001$). Although significant growth parameters emerged from this analysis, wherein the linear and cubic portions of the model were again evident, the addition of refractory status did not significantly aid in the prediction of the variability in the cubic growth pattern found.

Discussion

The first aim of this study was to confirm a measurement model of a summary maintenance factor constructed from the four additional maintenance factors described in Fairburn's and colleagues maintenance model (2003). The results of the CFA demonstrated that the four additional maintenance factors do share similar properties, and therefore all load well onto a common latent variable labelled here, a summary maintenance factor. In fact, the estimates calculated for this model indicate a very well-fitting model, suggesting that a common construct best represents these four factors. The confirmation that this model indeed exists amongst these variables has several beneficial implications. Mainly, the finding that these four factors can be combined to create a overarching latent variable that estimates the additional maintenance variables, opens many avenues for future research of this factor. From a clinical standpoint, the combination of these variables to describe a maintenance risk factor that could be used in assessment and ongoing treatment decisions could also be beneficial. As the measured variables that form the summary maintenance factor are all derived from the same self-

report questionnaire (EDI-2), the computation of this factor for clinical purposes can easily be derived and reported in a variety of clinical settings. Lastly, the emergence of a overarching factor that summarizes the theoretically driven variables described in the maintenance model (Fairburn, Cooper, et al., 2003) suggests that ED treatments directed at reducing any of the additional maintenance factors will have effects on the others, as these variables share common traits as factors involved in maintaining an ED.

The second objective of this study was to model the growth patterns of the summary maintenance factor over time and treatment. Using the summary maintenance factor score developed in the first aim of this study, an examination of the growth curves was performed. Results from this analysis confirmed a non-linear cubic growth pattern for the summary maintenance factor. More specifically, there was an increase in the summary maintenance factor level from intake to pre treatment, which was followed by a decrease to post treatment, which was subsequently followed by another increase during follow-up. This growth trajectory suggests that the intensive specialized treatments being offered to youth suffering with a moderate to severe ED are successful at decreasing those factors thought to be involved in maintaining an ED by post treatment. The results of this analysis also indicate that this growth curve applies to all types of EDs, revealing similar growth patterns transdiagnostically. Clinicians and treatment providers should continue to address similar issues in treatment as they are found to have therapeutic effects on these maintenance factors, across all ED categories. The increase in symptoms in the follow-up period suggests that treatment does not necessarily have lasting effects on the maintenance factors past the end of the treatment. Future studies should investigate what types of interventions would be more beneficial in sustaining the gains in the

maintenance factors that are achieved with treatment, such as offering a recovery group on an outpatient basis that focuses on the additional maintenance factors as one of its treatment components.

Another finding of the analysis of the growth trajectories is that a significant amount of variability existed in the cubic growth parameter, meaning that individuals in this sample had differing growth curves with regards to their summary maintenance factors. The last objective of this study was to explore whether refractory status could help explain some of the different trajectories found. Refractory status did not significantly predict the variability in the growth curves of the summary maintenance factor. This result suggests that the curves varied significantly across the 295 included in the study, but that refractory status did not help explain why these curves were differing across the individuals. Therefore, other factors are affecting how the progression of the maintenance factors differs across patients. Future studies should investigate other between-person predictors that may help explain some of the variability found in these curves. Predictors such as diagnosis, age, type of treatment received, and completion status would provide a good start to exploring this.

Limitations

Limitations of this study were the use of self-report measures, which in a disorder that is known for its egosyntonic properties (Vitousek, Watson, & Wilson, 1998), may have led to some under-reporting due to the denial component of the disorder. Other limitations concern the lack of longer follow-up periods to explore further growth of these trajectories, and the upper age limitation imposed when performing longitudinal investigations of adolescent samples. A further limitation were the few demographic

characteristics (i.e. ethnicity or socioeconomic status) that were not captured in the dataset, preventing any analysis of these demographics and their relation to the growth curves.

Future Directions

As one of the first studies to explore longitudinally the growth trajectories of the maintenance factors in a clinical sample of youth with EDs, much further research concerning this line of questioning is necessary to fully understand these phenomena. Future studies should strive to replicate the results of the CFA in both adult and non-clinical adolescent samples, in order to understand whether these factors merit conceptualization as part of a larger factor across all populations. In addition, future work should aim to examine growth curves over a number of different treatment encounters to learn more about treatment effects and lasting effects across different relapses. This would allow for the exploration of what occurs with each additional treatment encounter, and may help answer whether additional treatment is beneficial at providing therapeutic effects for the maintenance factors. Further, studies examining the growth curves of the maintenance factors into adulthood would also provide a more accurate account of what these growth patterns look like past adolescence, as this study was limited to a youth sample. Lastly, future studies should also aim to explore whether other demographic variables, such as diagnosis, age, or SES can help explain some of the variability in these growth curves. The addition of psychosocial variables, such as body dissatisfaction or ED chronicity as levels 2 predictors to help explain some of the variability found in the slopes would also be informative.

Conclusions

Growth curve analyses are a desirable statistical technique to study individual growth over time. In the current research, the exploration of the growth patterns of a summary maintenance factor across treatment and beyond illuminates our understanding of these factors and how they are related to refractory EDs. The combined additional maintenance factors of EDs do appear to follow a cubic growth pattern, wherein there is a slight increase in symptoms while waiting for treatment to begin, followed by a decline in symptoms with treatment, followed by a rebound of symptoms during follow-up. It is clear from these growth curves that the maintenance factors of adolescents with EDs do improve with intensive specialized ED treatment, although the lasting benefits of these treatments is still unclear. The need to have ongoing targeted treatment aimed at reducing impulsivity and perfectionism and increasing self-esteem and interpersonal trust in those adolescents at risk of a refractory ED, may decrease the need for a repeat visit, and shorten the length of a refractory course of illness.

Further, the findings of this study also provided some preliminary evidence that the levels of the summary maintenance vary across individuals. Although it was anticipated that refractory status may help explain some of that variability, it was not found to be a significant predictor. Other demographic and related variables should be examined for their role in explaining some of this variability. Much more research is strongly needed to fully understand the growth patterns of these maintenance variables, as these factors can be a key ingredient to understanding refractory EDs and what prolongs or maintains these devastating disorders.

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Table 1. Means and standard deviations of indicator variables according to timepoint.

Summary Maintenance Factor	N	Perfectionism	Interpersonal Distrust	Impulsivity	Ineffectiveness
Initial Intake assessment	272	7.03 (4.73)	5.43 (4.63)	6.57 (7.04)	10.86 (8.84)
Pre-treatment	256	7.13 (4.78)	5.48 (4.59)	6.61 (6.46)	11.00 (8.69)
Post-treatment	139	5.67 (4.39)	3.79 (3.79)	4.42 (5.00)	7.64 (7.38)
6 month follow-up	84	6.07 (4.87)	4.38 (4.62)	5.44 (6.27)	7.64 (7.38)
1 year follow-up	53	7.48 (4.82)	5.06 (4.51)	5.71 (5.86)	9.92 (8.36)

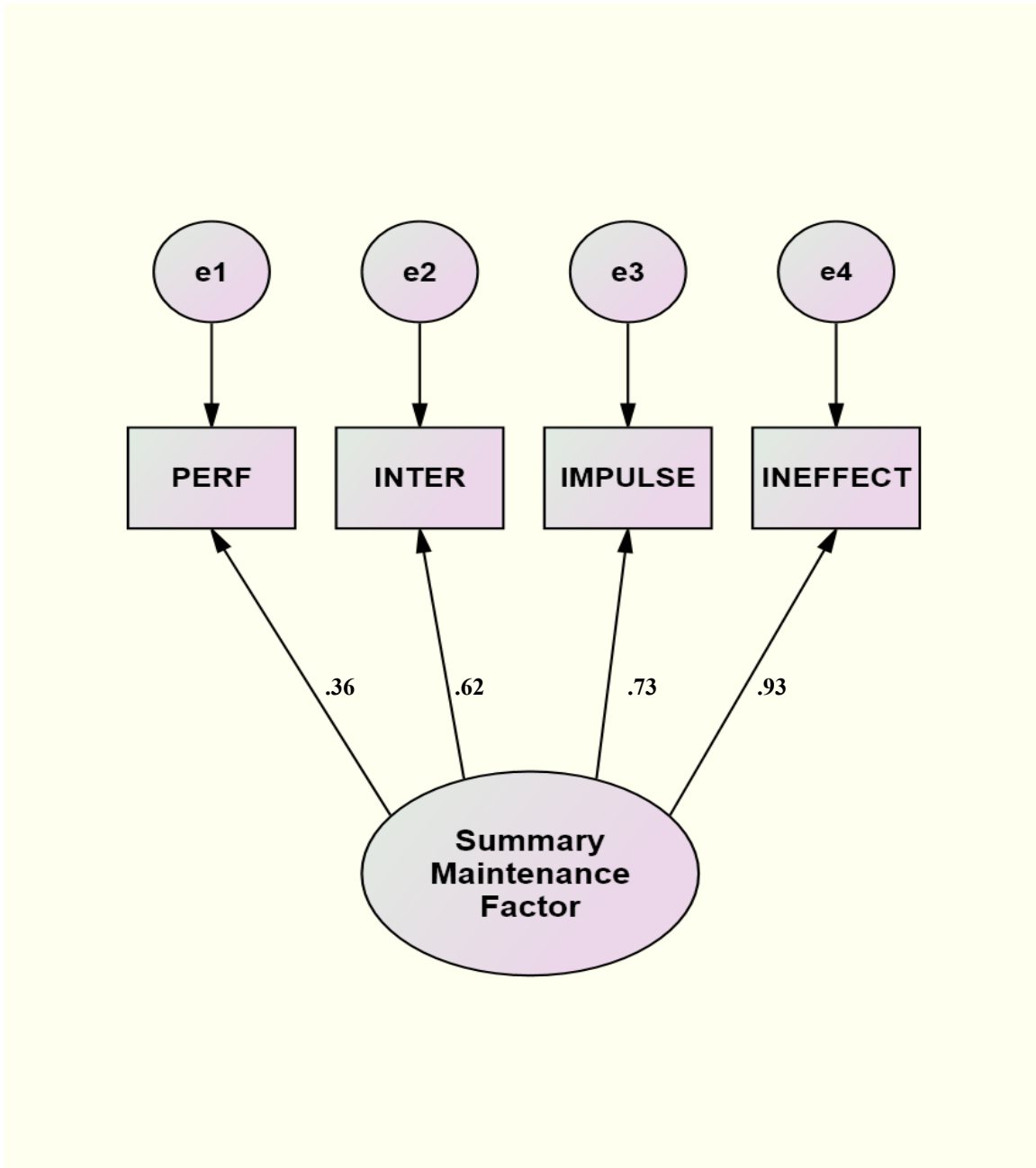
Table 2. Growth curve estimates for the summary maintenance factor

	Coefficient	Standard Error	<i>d.f.</i>	<i>t</i> -ratio	<i>p</i> -value
Fixed Effects					
Intercept, β_{00}	4.706	.197	269	23.832	< .001
Linear slope, β_{10}	-.524	.085	269	-6.191	< .001
Quadratic slope, β_{20}	-.015	.059	269	-.259	.796
Cubic slope, β_{30}	.328	0.62	269	5.278	< .001
	Standard Deviation	Variance	<i>d.f.</i>	χ^2	<i>p</i> -value
Random Effects					
Intercept, r_0	2.944	8.669	269	1576.266	< .001
Linear slope, r_1	.766	.586	252	335.253	< .001
Quadratic slope, r_2	.215	.046	137	161.934	.072
Cubic slope, r_3	.602	.362	51	171.047	< .001

Table 3. Growth curve estimates for the summary maintenance factor with refractory status as a time-invariant predictor

	Coefficient	Standard Error	<i>d.f.</i>	<i>t</i> -ratio	<i>p</i> -value
Fixed Effects					
Intercept, β_{00}	4.437	.229	268	19.410	<.001
REFstatus, β_{01}	1.012	.443	268	2.283	.023
Linear slope, β_{10}	-.631	.097	268	-6.470	<.001
REFstatus, β_{11}	.436	.192	268	2.272	.024
Quadratic slope, β_{20}	.017	.068	268	.252	.801
REFstatus, β_{21}	-.121	.135	268	-.893	.373
Cubic slope, β_{30}	.395	.072	268	5.513	<.001
REFstatus, β_{31}	-.262	.143	268	-1.837	.067
	Standard deviation	Variance	<i>d.f.</i>	χ^2	<i>p</i> -value
Random Effects					
Intercept, r_0	2.915	8.497	268	1540.547	<.001
Linear slope, r_1	.761	.579	251	330.739	<.001
Quadratic slope, r_2	.232	.054	136	164.627	.048
Cubic slope, r_3	.593	.351	50	167.666	<.001

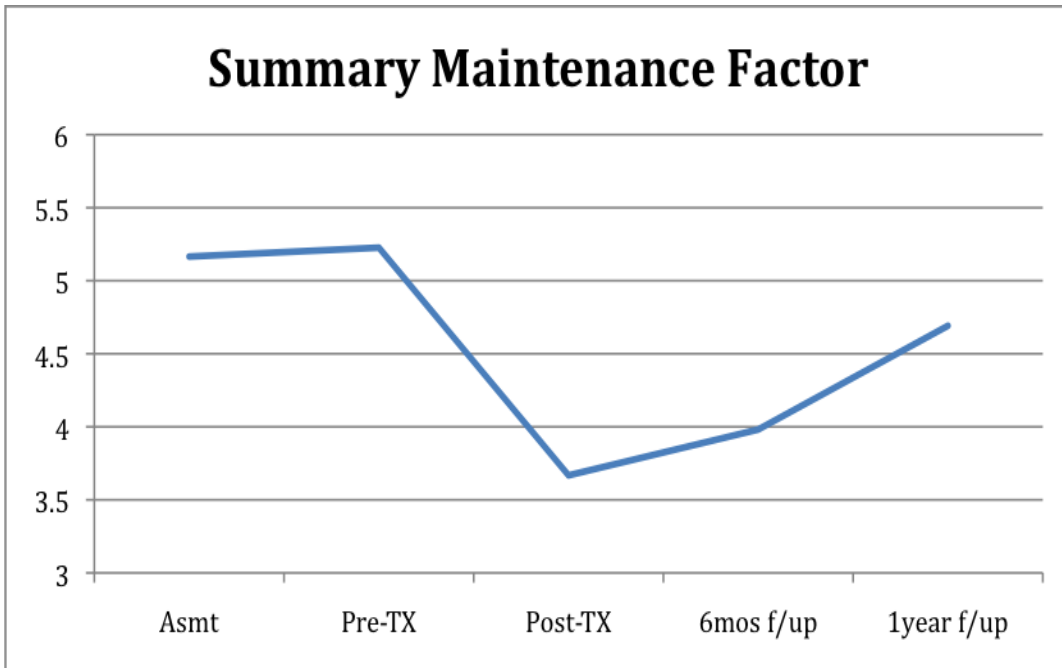
Figure 1. Standardized estimates of measurement model for the summary maintenance factor.



PERF=Perfectionism; INTER=Interpersonal Distrust; IMPULSE=Impulsivity;
INEFFECT=Ineffectiveness; N=324

$\chi^2(2)=1.506, p=.471$; CFI = 1.000; RMSEA = .000 (90% CI: .000 to .101)

Figure 2. Growth curve pattern of summary maintenance factor for full sample



General Conclusion

Refractory eating disorders (EDs) in adolescents are understudied and poorly understood. Despite the high prevalence rates of refractory EDs in this population (Richard, Bauer, & Kordy, 2005), and the multi-faceted severe consequences associated with a refractory course of illness (Kaplan & Strasburg, 2009; Strober, 2004), limited research still persists. The current project aimed to fill this significant gap in the literature, and proposed three main studies to better understand refractory EDs in an adolescent population. The objective of the first study was to explore predictors of refractory EDs. The goal of the second study was to examine whether unique profiles based on predictors from the first study, were capable of identifying single-episode versus different types of refractory groups. The third study examined the trajectories of a subset of predictors specifically implicated in the maintenance of an ED. This was performed in order to better understand how these predictors were involved in adolescent refractory EDs, both longitudinally and across intensive treatment. Together the three components of this research project provided a unique examination of refractory EDs in youth cross-sectionally and longitudinally, across treatment, and across different measurement points. As one of the first examinations of a transdiagnostic sample of adolescents with refractory EDs, these studies provide important preliminary evidence to guide healthcare professionals with assessment and treatment decisions, and also provide a foundation for which future research on refractory EDs in adolescents can be built.

One of the primary findings of this research is that a set of theoretically related predictors of refractory EDs assessed at initial intake, reliably predicted refractory status (single-episode versus refractory). This provides one of the first evidence-based accounts

of those characteristics that will allow clinicians to assess, very early on in presentation, which individuals may be more likely to suffer from a refractory course of the disorder. The results of this first study showed that an acute onset of the disorder, higher purging frequency, elevated levels of body dissatisfaction, and lower levels of depressed mood all significantly and uniquely added to the accurate prediction of refractory status. In addition, four further variables were included based on their affiliation as additional maintenance factors in Fairburn and colleagues (2003) transdiagnostic cognitive-behavioural maintenance model of EDs. Three of the four additional maintenance factors also emerged as unique significant predictors (ineffectiveness, interpersonal distrust and impulse regulation) while taking into account the other variables in the model, adding both strength and generalizability of these additional maintenance factors as active agents in refractory EDs in youth. Together these findings suggest that this set of predictors is useful in differentiating between single-episode and refractory cases, and that attention should be given to these variables at initial assessment as they have good predictive ability of the likelihood of a refractory ED in adolescents.

The results of the second study established that different profiles exist when examining the similarities amongst ED related and additional maintenance indicators. This study also revealed that regardless of whether you examine initial intake assessment data or residual change scores of pre to post change across the first treatment encounter, three types of groups exist. Although the profiles found across the two types of data were not synonymous, the resulting classifications suggest that three distinct profiles emerge when examining refractory and maintenance related variables together in a model. The implications of these classification results are significant in that they provide one of the

first depictions of the different types of profiles that exist in a clinical sample of youth with EDs when studying ED related and additional maintenance characteristics. Further, this study also allowed for a close look at how various data perspectives provide differing profiles. A comparison of two data captures concluded that how one progresses across the first treatment exposure versus predictors assessed at initial intake, provides more reliable and accurate identification of those at risk of suffering from a refractory ED. Therefore, progress indicators should be examined carefully by clinicians for identification of a refractory ED, and monitoring of those with poor progress across treatment should be made for early detection of the presence of a refractory ED.

The third study in this project examined the growth trajectories of the additional maintenance variables in a clinical sample of youth with EDs. This is the first longitudinal examination of Fairburn's (2003) maintenance model of EDs in a transdiagnostic adolescent sample. The findings revealed that a significant growth pattern existed for the maintenance trajectories, wherein there was a slight increase in these factors prior to treatment commencing, then a significant dip in these symptoms during the course of treatment, then a slight increase of these symptoms post treatment. These results suggest that intensive treatment is successful at reducing the effects of the maintenance variables, but that the lasting effects of this treatment on the maintenance variables have not yet been realized.

In reviewing the results of the three studies, several conclusions can be drawn. One of the major aims of this research project was whether it was possible to identify refractory cases of EDs at various points throughout treatment. The three studies allowed for the examination of different types of data, and to explore whether information from

the initial intake assessment, across the first treatment encounter or across 5 time points spanning treatment and follow-up periods, could reliably identify adolescents most at risk of a refractory ED. The findings across the studies demonstrated that initial intake assessment characteristics were helpful and significant at identifying those at risk of developing a refractory ED at an accuracy rate of 70%. This suggests that early identification of these cases is possible, and that those variables implicated in refractory EDs should be explored and considered during clinical assessments at initial intake.

Similarly, based on the results of the latent profile analysis of pre to post treatment scores, how an individual reacts or progresses through intensive ED treatment, also has some predictive value in identifying profiles of those with a possible refractory ED. Although this type of data is not considered necessarily helpful in quick identification of refractory cases, these indicators were better at identifying those at risk of a refractory ED than profiles at initial intake. As both presenting characteristics as well as progress data across treatment have been implicated in relapse and recovery studies (e.g. Castro et al., 2004; Hebebrand et al., 1997), findings of the current studies suggest that indicators at initial intake can reliably predict refractory status, but that it is profiles of how one progresses across the first treatment encounter that provide a better method of identifying adolescents who might suffer from a refractory ED. Therefore, in clinical settings, attention to both presentation characteristics as well as progress indicators could lend some important clinical information relevant to identification of refractory EDs in youth. Furthermore, the current studies also suggest that ongoing studies examining both types of predictors are warranted, as both types of predictors do provide useful, yet distinct, information regarding refractory EDs.

Another important finding of this project is the support found for Fairburn and colleagues' transdiagnostic cognitive-behavioral maintenance model of EDs (Fairburn, Cooper, et al., 2003). Very limited evidence exists regarding the applicability of this model to youth with EDs, with only one study performed to date that investigated this model in a community sample of youth with binge eating disorder (Allen, Byrne, & McLean, 2012). Furthermore, as this model is postulated to be transdiagnostic in its application, only a couple of adult studies examining this model in various ED diagnoses has been performed (Lampard, Byrne, McLean, & Fursland, 2011; Tasca et al., 2011). Thus, the addition of the current studies to compliment the limited evidence examining this model, provides a unique application of this model to a large transdiagnostic sample of youth with an ED. Findings of this research relate to the generalizability of this model to youth samples, and speaks to the developmental applicability of the additional maintenance variables in adolescent refractory EDs. The findings across the project also allow for discussion regarding the transdiagnostic nature of refractory EDs. As all types of EDs were included in this research, the applicability of the findings to all three major ED categories is warranted. Future studies should continue to be conducted in large transdiagnostic samples, and the investigation of diagnostic effects in youth samples would be a good next step.

In addition, research investigating other developmentally relevant constructs that may also be involved in adolescent refractory EDs, would be beneficial to fully understand the appropriateness of this model to younger samples. As constructs such as attachment (Illing, Tasca, Balfour, & Bissada, 2010) and parental self-efficacy (Lafrance Robinson, Strahan, Girz, Wilson, & Boachie, 2012) have been implicated in ED

recovery; the addition of these variables may provide a more comprehensive picture of how these variables affect refractory EDs in youth. Lastly, the confirmation that the four additional maintenance factors involved in this model do reliably map onto a larger construct in youth samples provides a valuable method in which to study these characteristics in combination. Future research in various types of clinical and community-based samples should strive to confirm the generalizability of this measurement model, thus allowing for greater conclusions about the cohesiveness of these factors in representing a larger conceptual construct. The clinical and research benefits of such a construct could be used to better understand refractory EDs and for tailoring of treatment goals towards reducing the effects of these maintenance variables.

Other clinical implications of this work are linked to early identification and treatment progress of characteristics theoretically related to refractory EDs. Primarily, this research project demonstrated that refractory EDs can be identified early on in treatment, and therefore attention to these constructs at early points of treatment should be made. Identification of those cases at risk of a refractory course of illness has multiple implications for the treatment provider, in that it allows for the tailoring of interventions towards the factors thought to maintain the disorder. Furthermore, for those individuals who are at greatest risk of suffering from a refractory ED, treatment aimed at working on interpersonal trust, impulsivity, and lifting self-esteem, could reduce the amount of treatment required or the need for a return to treatment. Although the results that emerged from the growth trajectory analysis suggest that intensive treatment is effective at reducing maintenance factors of EDs, it also reveals limited lasting effects. This suggests that longer-term interventions geared at addressing the additional maintenance factors,

such as the use of outpatient recovery groups, are needed to continue the therapeutic effects gained during intensive treatment.

Further, the use of the operational definition of refractory EDs as those who require more than one same-type treatment, allows for a reliable and valid method of identifying these cases. This research provides some preliminary evidence that this definition is adequate at summarizing this subgroup of EDs, with evidence that initial intake variables could accurately differentiate between these two types of patients. Further evidence that this definition is reliable, is that the latent profile analyses revealed significant association of this refractory status and those who do poorly at treatment, lending some justification that this group will require a return to treatment. Thus, future studies should attempt to replicate the use of this definition in varying samples, in order to confirm whether this operational definition merits consideration as a global method in which to define this type of patient.

In summary, although part of the original hypothesis of this work was that factors theoretically found to be involved in maintaining an ED would also differentiate between different types of refractory EDs (recurrent versus chronic), the results of these studies failed to find evidence that this is possible in the early stages of treatment. It may be possible that either the chronicity of the disorder builds over time, or that it is exposure to multiple treatment encounters that leads to the differing type of refractory EDs. Also, due to the ceiling effects of conducting research with pediatric samples, it may also be possible that the differentiation between the types of refractory EDs is not evident until adulthood. Nonetheless, future longer-term studies that transcend through the developmental periods are necessary to fully explore this phenomenon. Future research

should also aim to examine a more developmentally appropriate model of Fairburn's and colleagues (2003) model, potentially including constructs of attachment and parental efficacy in order to fully understand whether these constructs more accurately depict refractory EDs in youth samples. Further, applying this model to other disorders such as obesity in pediatric samples may also shed some light of how individuals are affected by these constructs.

Understanding refractory EDs and their trajectories, and being able to identify those who are most at risk of suffering from this course of illness may provide benefits to the patient, their families, and to the treatment team and healthcare system (Goldstein et al., 2011; Richard et al., 2005; Strober, 2004) by shortening the course of this illness. Much more work is necessary before firm conclusions could be made about adolescent refractory EDs, but this research provides some preliminary evidence that refractory EDs are prevalent in these populations and that attention should be devoted to learning how best to identify and treat these cases. With estimates in this large transdiagnostic adolescent sample of EDs finding that approximately 30% of adolescent cases will require anywhere between 2 to 6 treatment encounters for alleviation of symptoms of their ED, it is essential that researchers and clinicians make a concerted effort to understand how best to identify and manage these difficult and complicated cases.

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