Predicting Treatment Outcome in Individuals With an Eating Disorder

Eva Vall

A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy (Clinical Psychology)

School of Psychology
Faculty of Social and Behavioural Sciences
Flinders University

March 2016

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ABSTRACT

Eating disorders are serious and prevalent mental disorders that are associated with significant impairments across both physical and psychological domains. Achieving good treatment outcomes is an important goal for this group, but many patients do not improve significantly with treatment. At present, it is not clear which factors can best distinguish those who are likely to respond well versus those who are not. The purpose of this thesis was to improve our understanding of what predicts outcome in individuals receiving treatment for an eating disorder.

The first study was an investigation into the current evidence base, and included a comprehensive review and meta-analysis. The most robust predictors of treatment outcome that emerged were early change in symptoms during treatment and baseline motivation. A number of key gaps and limitations across the literature were identified. These included an absence of testing of theoretically informed models with appropriately sophisticated statistical analyses, few investigations into transdiagnostic predictors, and a wide variability in how outcomes were measured. Three empirical studies were subsequently undertaken to address these limitations, and were additionally guided by prominent theoretical models of eating disorders. These models suggested that perfectionism/cognitive rigidity, mood intolerance and ineffectiveness were potentially important predictor variables.

In order to validate a measure of cognitive rigidity, the second study examined a computerized version of the Trail Making Test (assessing set-shifting) in a transdiagnostic sample of inpatients with an eating disorder.

For the remaining empirical studies (third and fourth studies), two treatment samples were obtained. The first consisted of adolescents with anorexia nervosa (AN) who were inpatients in a specialist paediatric unit. Change in two predictor variables during treatment predicted outcomes: greater weight change during treatment predicted greater

increases in body mass index (BMI) centile by follow-up, and increased personal standards perfectionism during treatment predicted a greater likelihood of being readmitted within 3 months of discharge. There were interactions between time and driven exercise (higher levels of baseline exercise resulted in a lower BMI centile at follow-up) and set-shifting (faster set-shifting was associated with poorer quality of life at discharge and follow-up). In terms of simple baseline predictors, higher purging, concern over mistakes perfectionism, emotional regulation difficulties, and faster set shifting were associated with higher levels of eating disorder pathology and poorer quality of life over all points of follow-up.

The second sample was transdiagnostic, and consisted of adults admitted to a short-term stay specialist inpatient eating disorder unit. Diagnosis did not predict any outcome measure, with the expected exception of weight change. Individuals with more severe eating disorder symptoms made greater improvements in disordered eating by follow-up, but remained at a higher overall level of illness severity. Greater improvement in symptoms during treatment was associated with greater improvement at follow-up. Baseline concerns over mistakes moderated the relationship between improvements in quality of life as an inpatient and improvements in quality of life at follow-up. For those with anorexia nervosa, a longer duration of illness predicted less improvement in BMI at follow-up, while improvements in quality of life during treatment predicted greater improvements in BMI by follow-up.

Taken together, these findings suggest that across age-groups, encouraging robust symptom change during treatment is likely to result in improved outcomes. While our results provide preliminary support for the selected theoretical predictors, further research in more controlled settings is needed to better understand their contribution to outcomes. Perfectionism appears to warrant particular investigation as a target for therapeutic intervention that could have clinical benefit.

DECLARATION

I certify that this thesis does not incorporate without acknowledgement any material previously submitted for degree or diploma in any university, and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

Eva Vall

BA (Hons)

ACKNOWLEDGEMENTS

I feel extremely fortunate to have had the opportunity to devote the past 3 years to this research, which has been an overwhelmingly rewarding experience. I would particularly like to thank the following people for making it so:

Heartfelt thanks goes to my supervisor, Professor Tracey Wade. Your passion and commitment to advancing the field of eating disorder treatment and research has certainly washed off on me, and helped me enormously in my development both as a researcher and as a clinician. I count myself extremely lucky to have had the opportunity to be part of your lab. Thank you for your guidance, insights and support throughout the entire process, and for your sage words at times when they were needed!

Sincere thanks to the staff in the eating disorder wards at Flinders Medical Centre. At Ward 4GP, thanks to Randall Long for endorsing and supporting the research, and to the nursing staff for accommodating my presence and helping to facilitate two long years of data collection! Thanks also to Mandy Yiu and Michael Batterham in the Paediatric Inpatient Unit for their willingness to have me conduct this research in an already very busy clinical setting. And to Sandy Bridgland who greatly facilitated data collection by keeping me up to date on admissions and discharges.

Thanks to Ben Maddock for helping to set-up up the electronic assessments, and for providing system maintenance and trouble-shooting support along the way.

Huge thanks to my parents Lilla and Nick for so carefully helping with proof reading – the thesis reads much better because of it! And of course, thank you to my wonderful husband Elliot, for your constant calm support throughout this long endeavour.

Finally, I would like to thank every participant who took part in this research. I am deeply grateful for your willingness to be involved, and for so graciously giving your and time and energy to completing the assessments. I hope this research will go a small way towards improving the treatments on offer in South Australia in the future.

Chapter 1

Overview and Aims of the Research

1.1 Background and Context

Eating disorders are severe and debilitating illnesses that affect a substantial portion of the population, particularly women. The most prevalent of these disorders included in the current Diagnostic and Statistical Manual of Mental Disorders (DSM-5: American Psychiatric Association [APA], 2013) are anorexia nervosa (AN), bulimia nervosa (BN), binge eating disorder (BED) and other specified feeding and eating disorders (OSFED). AN is characterised by low body weight (generally considered to be <85% of expected for age and height), body image disturbance or undue influence of body shape or weight on self-evaluation, and fear of weight gain. A diagnosis of BN requires objective binge episodes and attempts to redress the effects of binge eating (i.e., purging [vomiting, laxatives, diuretics], fasting, or excessive exercise) to occur on average once a week, accompanied by an undue influence of body shape or weight on self-evaluation. BED shares the same binge eating features as BN, but without the associated compensatory behaviours. OSFED is diagnosed where one or more of the diagnostic criteria for AN, BN or BED are absent, or below specified frequency. Two additional diagnoses, namely purging disorder and night eating syndrome, are also included under the OSFED umbrella. Evidence suggests that OSFED disorders are associated with levels of disability commensurate with the other eating disorder diagnoses (Zimmerman, Francione-Witt, Chelminski, Young, & Tortolani, 2008).

Several other feeding and eating disorders which more commonly commence in childhood are also included in the current diagnostic criteria (APA, 2013), including pica, rumination disorder and avoidant/restrictive food intake disorder. Given that these three feeding and eating disorders were only linked with DSM eating disorders from 2013, we know much less about these compared to AN, BN, BED and OSFED. Accordingly, the focus of the current research is on the four disorders highlighted in the first paragraph.

The combined lifetime prevalence of AN, BN, BED and OSFED by age 20 is estimated at around 13% (Fairweather-Schmidt & Wade, 2014; Stice, Marti, & Rohde, 2013). Disordered eating is accompanied by significantly lower quality of life (both physical and psychological) compared to women without disordered eating (Ágh et al., 2016; Wade, Wilksch, & Lee, 2012). BN and AN are the 8th and 10th greatest cause of disease burden (respectively) in 15 to 24 year old women (Australian Institute of Health and Wellbeing, [AIHW], 2007). Mortality related to all causes is the highest across all psychiatric disorders (Crow et al., 2009; Harris & Barraclough, 1997). At the service level, eating disorders are associated with high health care use and represent a substantial burden on health services (Ágh et al., 2016; Mond, Hay, Rodgers, & Owen, 2007). This is partly due to the high economic impacts associated with inpatient treatment, a frequent but costly necessity in the treatment of eating disorders (Striegel-Moore et al., 2008; Thompson et al., 2004). Moreover, this cost tends to fall on public health systems, with around 90% of inpatient admissions for AN being to public hospitals (AIHW, 2011).

Given the adverse impacts of eating disorders on individuals and health systems alike, effectively treating sufferers is an important goal, and significant efforts have been invested into developing specialized interventions. For BN and BED evidence supports the efficacy of individual psychological therapy and cognitive-behavioural approaches (Hay et al., 2014; Wilson & Shafran, 2005). For adolescent AN family-based treatments have the strongest evidence base, while renourishment with the addition of psychotherapy appears to be the most effective combination for adults (Watson & Bulik, 2013). Although outpatient treatments are considered the first-line approach across the eating disorder spectrum, inpatient treatment is often essential to protect physical wellbeing, particularly when there are serious medical complications or where outpatient treatment is not successful (Hay et al., 2014).

1.2 Aims of the Current Research

Despite the emergence of specialist eating disorder interventions, outcomes for many patients who receive treatment remain sub-optimal. For adults, conservative recovery rates approximately one year post-treatment have been reported at less than 30% for AN and BN (Keel & Brown, 2010), while for both adults and adolescents, even the most optimistic estimates suggest that around 25% of individuals will retain their eating disorder symptoms up to 15 years after treatment (Herzog et al., 1999; Strober, Freeman, & Morrell, 1997). In order to improve the existing treatment response rates, it would be useful to understand the factors associated with the differential response patterns of this patient population. At the simplest level, such insights provide important prognostic information that could guide the delivery of individually tailored or targeted interventions, or identify patients who are at risk of poor outcomes and require more assertive follow-up. At the next level, understanding what predicts outcome could help to inform the development of more effective treatment approaches, as it identifies those variables and processes that warrant further examination in intervention research.

Unfortunately, our ability to implement such improvements is currently hampered by a limited understanding of the factors associated with treatment outcome. The purpose of this thesis is therefore to improve the current understanding of what predicts treatment response in patients with an eating disorder. Specifically, it sets out to address two key aims:

1. Determine the current status of predicting outcomes for patients who receive treatment for an eating disorder, including the major gaps and limitations.
2. Investigate theoretically indicated predictors within an adult and an adolescent clinical sample.

In order to address these aims, four studies were conducted. These appear in this thesis as individual chapters, and are described briefly below.

1.3 First Study

The first study **(Chapter 2)** is a comprehensive literature review and meta-analysis. Material from this chapter has been published in the *International Journal of Eating Disorders* (Vall & Wade, 2015). The purpose of this study was to critically synthesise the existing body of literature on this topic. Notably, at the time of submission of this thesis, it was the only meta-analysis to be conducted in this area, providing an additional level of evaluation of the magnitude of the effect of each predictor. Additionally, it extended the insights made by previous reviews in two ways. First, it was transdiagnostic in scope, examining predictors of outcome in individuals with AN, BN, BED and OSFED. Second, it considered both adult and adolescent studies. The study also provided a comprehensive, updated summary of the limitations of knowledge in the field. These included a relative absence of testing complex, theory-driven predictors, large variability in how outcomes were measured across studies, and few studies of transdiagnostic predictors. These limitations guided the development of the subsequent approach used in this thesis.

1.4 Second Study

One of the variables identified in the first study as deserving further examination was neurocognitive functioning. One facet of this, namely cognitive inflexibility, is further indicated across several theoretical models of eating disorder maintenance, however its measurement has not been fully established in routine settings. In order to validate such a measure for use in the subsequent studies, the second study (**Chapter 3**) examined the validity of a freely available computerized version of the Trail Making Test (assessing set-shifting as an indication of cognitive inflexibility) for people with eating disorders. This study also served to investigate the set-shifting abilities of individuals with BN, an area which has been little studied to date. Material from this chapter has been published in the *European Eating Disorders Review* (Vall & Wade, 2015)**.**

1.5 Third and Fourth Studies

The third and fourth studies (**Chapters 4 and 5**) investigated predictors of outcome in two different inpatient groups (adult and adolescent). It is widely accepted that theoretically informed processes should always be part of the evaluation of complex clinical interventions such as those in the present treatment settings (Campbell, Fitzpatrick, Haines, & Kinmonth, 2000; Craig et al., 2008), however an absence of testing theoretically driven predictors emerged as a significant limitation in the first study. To address this, variables from prominent theoretical models were chosen to guide the analyses conducted in this thesis.

First, the *Transdiagnostic Model* (Fairburn, Cooper, & Shafran, 2003) proposes that at the core of all eating disorders is an individual's over-evaluation of eating, shape and weight and their belief about the extent to which they can control these factors. Subsequently, the key maintaining factors of eating disorder symptomatology are clinical perfectionism, core low self-esteem, mood intolerance and interpersonal difficulties. These maintaining factors have been shown to predict dietary restraint in a clinical sample (Hoiles, Egan, & Kane, 2012), and the model is further supported by the reported efficacy of treatments based on the model both with adults (Byrne, Fursland, Allen, & Watson, 2011; Fairburn et al., 2015; Fairburn et al., 2013) and adolescents (Dalle Grave, Calugi, Doll, & Fairburn, 2013; Dalle Grave, Calugi, Sartirana, & Fairburn, 2015).

Second, the *Three-Factor Model* (Bardone-Cone, Abramson, Vohs, Heatherton, & Joiner Jr, 2006) posits that the interaction of high perfectionism, low self-efficacy, and weight/shape concern, serves to maintain and increase bulimic and compensatory symptoms. This model has received mixed empirical support in clinical samples, with one follow-up study (Bardone-Cone et al., 2008) finding that the model was a viable predictor of bulimic symptoms. In another study, the model predicted binge eating but not compensatory behaviours in one study (Bardone-Cone et al., 2006), and another attempted

replication found that the model was unsuccessful in predicting either binge eating or purging (Watson, Steele, Bergin, Fursland, & Wade, 2011).

Finally, the *Cognitive-Interpersonal Maintenance Model* (Schmidt & Treasure, 2006) was developed with respect to AN only. Unlike the other two models, this model is 'culture free', in that it does not emphasise the role of weight or shape-related factors in the maintenance of the disorder. Instead, the interpersonal component of the model highlights the importance of carer response to the illness in exacerbating symptoms, while the cognitive component proposes that perfectionism/cognitive rigidity, experiential avoidance and pro-anorectic beliefs further help to maintain eating disorder symptoms. A comprehensive test of the whole model has not been undertaken, but the interpersonal components were found to predict symptoms in inpatients with AN (Goddard et al., 2013), and evidence for the individual cognitive factors in the model is accumulating (Treasure & Schmidt, 2013). To date, the model has not been examined in transdiagnostic samples.

Given the large number of potential maintaining factors indicated across the three models, the scope of this thesis did not enable a thorough testing of each model, nor an examination of every variable suggested by the models. Moreover, the clinical setting in which the present research was conducted required that patient-burden be carefully considered. Accordingly, it was decided that those variables that are shared across all three models guide the empirical focus of this thesis, namely clinical perfectionism, low self-esteem/self-efficacy, and mood avoidance/intolerance. In addition to these theoretical predictors, a number of predictors that emerged as important in the meta-analysis were also examined. These included change in symptoms during treatment, baseline symptom severity, motivation to recover, demographic variables and behavioural features such as binge/purge frequency and driven exercise.

In order to properly evaluate and advance interventions, it has also been suggested that an understanding of *how* variables influence outcome is essential (Michie &

Prestwich, 2010). This involves the examination of complex predictive processes (including moderators and mediators) the absence of which was similarly identified as a limitation in the first study of this thesis. Accordingly, complex predictive analyses were included throughout all the present studies.

Finally, to ensure a robust and consistent approach to defining outcomes, a comprehensive range of measures were used, including change in eating pathology, change in eating disorder related quality of life and change in weight for underweight patients. In addition, given the high economic costs associated with eating disorder treatment, understanding how to achieve satisfactory patient outcomes while also improving service-level efficiencies is also an important goal. Accordingly, two outcomes that have implication at both the patient and service levels were also considered, namely drop-out from treatment and readmission to hospital.

1.5.1 Predicting outcomes in adolescents with AN.

The third study **(Chapter 4)** examined predictors of outcome in adolescent inpatients. Data were collected over a 12-month period from an inpatient unit that only admits patients who are medically unstable, thereby limiting our analyses to adolescents with AN. In terms of simple baseline predictors, higher purging, concern over mistakes perfectionism, emotional regulation difficulties, and faster set shifting were associated with higher levels of eating disorder pathology and poorer quality of life over all points of follow-up. Change in two predictor variables during treatment predicted outcomes: greater weight change predicted higher BMI centile at follow-up, and increased perfectionism predicted a greater likelihood of being readmitted within 3 months of discharge. Variables that interacted with time included driven exercise (higher levels of baseline exercise resulted in a lower BMI centile at follow-up) and set-shifting (faster set-shifting was associated with poorer quality of life at discharge and follow-up). This study has been peer reviewed and accepted for publication in *Clinical Psychologist* (Vall & Wade, in press).

1.5.2 Predicting outcome in a transdiagnostic adult sample.

The final empirical study (**Chapter 5)** was conducted with a sample of transdiagnostic adult inpatients. Data were collected over a 24-month period from a short-stay eating disorder unit. All identified predictors were transdiagnostic in scope, with the expected exception of those predicting change in BMI, which were examined in individuals with AN only. Higher eating disorder symptom severity at baseline predicted a greater magnitude of symptom change by follow-up, however individuals with higher baseline symptoms nonetheless remained at a higher overall level of severity at all time points. A similar, albeit less robust, trend was apparent for individuals with higher levels of concern over mistakes perfectionism. Greater improvements in eating disorder pathology and quality of life during treatment predicted larger improvements in these respective outcomes at follow-up. Baseline concerns over mistakes moderated the relationship between improvements in quality of life during treatment and improvements in quality of life at follow-up. For individuals with AN, improvement in BMI during treatment did not predict change in BMI at follow-up, but improvement in quality of life was associated with greater improvement in BMI at follow-up. This study was recently peer reviewed by the *International Journal of Eating Disorders,* and has subsequently been revised and resubmitted based on reviewer comments. The version that appears in this thesis incorporates the changes made in response to reviewer feedback.

1.6 Implication of the Findings

The final chapter of this thesis (**Chapter 6)** provides a compressive discussion which integrates the findings of the four studies included in this thesis. Further, the discussion summarises the key contributions of this thesis to the broader subject area, considers the strengths and limitations of the research, and provides a detailed discussion of the clinical, theoretical and methodological implications of the current findings.

1.7 A Note on the Thesis Including Published or Submitted Works

All chapters in the thesis were prepared as manuscripts. As the manuscripts were prepared for different journals, their formatting varies slightly, and the chapters include some of the same basic background information and methodology.

In addition, the peer review process revealed a wide diversity of opinions about how analyses should be conducted, both at the theoretical and methodological levels. Notably, the reviewers of the adult and adolescent manuscripts had different opinions about the appropriate approach. Therefore, although the research for both the adolescent and adult samples was initially executed in a consistent manner, the review process resulted in a number of differences that are apparent in the final versions of the manuscripts. In particular, this resulted in different methodological approaches to the analyses, and significantly less variables being included in the adult manuscript. The implications of the range of preferred and accepted methods favoured by different experts for the ongoing development of this area of research are discussed in detail in the final chapter of this thesis.

Chapter 2

Systematic Literature Review and Meta-Analysis[1]

[1] Material from this chapter has been published in the *International Journal of Eating Disorders* [Vall, E., & Wade, T. D. (2015). Predictors of treatment outcome in individuals with eating disorders: A systematic review and meta-analysis. *International Journal of Eating Disorders, 48*(7), 946-971.]

2.1 Abstract

Objective*:* Understanding the factors that predict a favourable outcome following specialist treatment for an eating disorder may assist in improving treatment efficacy, and in developing novel interventions. This review and meta-analysis examined predictors of treatment outcome and drop-out.

Method: A literature search was conducted to identify research investigating predictors of outcome in individuals treated for an eating disorder. We organized predictors first by statistical type (simple, mediational and moderational), and then by category. Average weighted mean effect sizes (*r*) were calculated for each category of predictor.

Results*:* The most robust predictor of outcome at both end of treatment (EoT) and follow-up was the mediational mechanism of greater symptom change early during treatment. Simple baseline predictors associated with better outcomes at both EoT and follow-up included higher BMI, fewer binge/purge behaviours, greater motivation to recover, lower depression, lower shape/weight concern, fewer comorbidities, better interpersonal functioning and fewer familial problems. Drop-out was predicted by more binge/purge behaviours and lower motivation to recover. For most predictors, there was large inter-study variability in effect sizes, and outcomes were operationalised in different ways. There were generally insufficient studies to allow analysis of predictors by eating disorder subtype or treatment type.

Discussion: To ensure that this area continues to develop with robust and clinically relevant findings, future studies should adopt a consistent definition of outcome and continue to examine complex multivariate predictor models. Growth in this area will allow for stronger conclusions to be drawn about the prediction of outcome for specific diagnoses and treatment types.

2.2 Introduction.

Identifying predictors of outcome is an important goal in the quest for improving outcomes in eating disorder treatment, where outcomes remain sub-optimal even after intensive intervention (Keel & Brown, 2010). This is particularly true of outcomes related to receiving specialist treatment for an eating disorder (as opposed to naturalistic follow-up in the absence of an intervention) as, at the individual level this would allow us to identify those people who are most at risk of a poor outcome. This knowledge could be used to offer more targeted or intensive interventions to these individuals and to ensure that their long-term follow up is given priority. In the wider sense, knowing which factors affect treatment outcome is valuable because it offers specific insights into how treatments for eating disorders can be improved. Identification of factors that impede progress can inform the modification of existing treatments, or the development of future interventions.

Despite the promise of this kind of approach, there is a well-documented paucity of robust and consistent findings related to predictors of response to treatment in eating disorders. While to our knowledge no systematic review of predictors of response to specialist treatment across eating disorders exists, several reviews of treatment outcomes more generally have considered this question. One review of anorexia nervosa (AN) treatment studies (n = 35) (Bulik, Berkman, Brownley, Sedway, & Lohr, 2007) attempted to identify sociodemographic predictors of treatment outcome, but found that evidence to support the predictive value of any factors linked to AN treatment outcome was weak. Several predictive factors for outcome for bulimia nervosa (BN) were identified in a review of randomised controlled trials (n = 47) for BN treatment, including more frequent binge eating and longer illness duration (Shapiro et al., 2007). However, these effects were found for individuals receiving behavioural interventions and did not extend to medication trials. A more recent review of treatment studies (n = 79) of bulimia nervosa (BN) treatment arrived at similar conclusions, noting that although significant research efforts had been invested in this area, it had failed to identify consistent prognostic factors

(Steinhausen & Weber, 2009). Another review of studies (n = 62) that considered outcomes for both AN and BN (Berkman, Lohr, & Bulik, 2007) rated several factors as 'moderately successful' in predicting poorer treatment response, namely the presence of mood and anxiety disorders and impaired social functioning. It should be noted, however, that several studies included in the review were based on findings with participants who had been identified through community screening or assessment, and some of these people may not have received specialist treatment. Accordingly, for these studies it cannot be concluded that the predictors of outcome were associated with treatment *per se*, or whether they simply reflected the normal course of eating disorders. The results of a European collaboration involving over 2000 patients with either AN, BN or OSFED, treated across 12 countries in 80 treatment centres, suggested that greater symptom severity might be associated with a poorer outcome at 12 month follow-up (Richard, Bauer, & Kordy, 2005). However, there are numerous challenges inherent across such a trial, where naturalistic data are collected over multiple sites. These include potential differences across sites in recruitment, treatment, participant characteristics, and assessments, and findings must therefore be interpreted with caution. Finally, a review of randomized controlled trials for BED (n = 26) concluded that evidence to support specific predictors was 'sparse' (Brownley, Berkman, Sedway, Lohr, & Bulik, 2007). Moreover, all the reviews noted that sample sizes varied widely across studies.

Drop-out from treatment has also been studied as a specific type of outcome in the eating disorder field, and one review has specifically investigated predictors of drop-out (Fassino, Piero, Tomba, & Abbate-Daga, 2009). This review examined studies (n = 26) reporting factors associated with drop-out from treatment for all eating disorders and noted several predictors, including the binge/purge subtype of AN, styles of personality (i.e., low self-directedness and low cooperativeness), and psychological traits (i.e., high maturity fear and impulsivity). However, the authors noted that the ability to draw meaningful

conclusions was hampered by methodological limitations across the studies, including small sample sizes and lack of replication of findings. A second review of studies (n = 7) reporting drop-out from treatment for AN (Wallier et al., 2009) concluded that evidence to support the presence of robust predictors was both scarce and conflicting, but also found some evidence that individuals exhibiting more binge/purge behaviours were less likely to complete treatment. As in the reviews of treatment outcome, sample sizes varied widely across studies included in the reviews of treatment drop-out.

Since the publication of the most recent reviews in 2009, a number of studies have emerged that have included at least some analysis of predictors of treatment response. The purpose of this review and meta-analysis is to systematically examine the existing literature across all eating disorders and present a rigorous summary of the evidence for predictors of treatment outcome in individuals with an eating disorder. In addition, it extends the insights offered by previous reviews in several ways. First, to our knowledge, no meta-analysis of predictors of treatment outcome or drop-out has been conducted, which limits the capacity to draw conclusions about the importance and clinical significance of potential predictors given different (i) numbers of studies examining any one predictor, and, (ii) varying sample sizes. Second, none of the reviews has investigated more complex predictor models, such as interactions between predictors, moderator or mediator effects. In this review, predictors are categorized first by the type of relationship they have with outcome (simple, mediational and moderational), and then by type. Third, it examines both predictors of drop-out from treatment and predictors of improvement after receiving specialist treatment for an eating disorder. Fourth, in line with the inclusion of binge eating disorder (BED) in the DSM-5 (APA, 2013), this is the first review of predictors of treatment outcome that has included AN, BN and BED in one review, which is consistent with the trend to attempt to identify commonalities across diagnoses in order to inform transdiagnostic treatment approaches (Dalle Grave et al., 2013; Fairburn et al.,

2003; Wade, Bergin, Tiggemann, Bulik, & Fairburn, 2006). Finally, given the large number of studies being conducted in the area, methodological issues that continue to limit the usefulness of findings in this area are examined and these considerations are consolidated to provide recommendations to improve the design of future treatment studies that also intend to examine predictors of outcome.

2.3 Method

2.3.1 Information source and search strategy.

The present study was conducted in accordance with the evidence-based guidelines for systematic reviews set forth in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA: Liberati et al., 2009).

The primary search strategy involved searching peer reviewed published papers using a multi-field search in two databases, namely PsycINFO and PubMed. The final database search was conducted on 26 December 2014.

The following combinations of search terms were employed where the terms appeared in either the title or abstract of the article:

1. anorexia OR bulimia OR binge eating disorder OR eating disorder

   AND

2. treatment

   AND

3. response OR outcome

   AND

4. predictor OR predict OR mediator OR mediate OR moderator OR moderate

The secondary search strategy involved identifying relevant papers from the reference lists from papers identified in the primary search.

2.3.2 Inclusion criteria.

The following specifications were applied: (i) English-language publication, (ii) eating disorder diagnosis, (iii) specialist eating disorder treatment, and (iv) published in a

peer-reviewed journal. The search was limited to articles published in the last 30 years (i.e., since 1984).

2.3.3 Study selection.

Prior to examining the results, the search outputs from the two databases were first cross referenced and all duplicate records were removed. Next, the abstract of every record was reviewed to ensure that the inclusion criteria were met, and that the study related broadly to the review question. The full-text of all remaining records was examined to confirm eligibility in the qualitative synthesis. Finally, all studies were screened for inclusion in the meta-analysis, including the calculation of effect sizes. Studies were excluded if there was insufficient data to calculate an effect size. The authors discussed any studies where there was uncertainty about inclusion, and studies were only included if both authors agreed that they met inclusion criteria. A flow diagram of the selection process based on the PRISMA guidelines is presented in **Figure 1**.

2.3.4 Data extraction.

For each category of predictor, data was extracted from all studies addressing that variable, as shown in **Table 1**. This included the type of study (i.e., randomized controlled trial or case series), eating disorder subtype, the number of individuals included in the analysis of the particular predictor, specific type of treatment(s) administered, an operationalised description of the outcome variable, the outcome period, and the specific predictor measure.

2.3.5 Categorising predictors of treatment response.

For this study, predictors were categorised first in terms of the way in which they contribute to outcome, or their relationship with the outcome variable. To this end, predictors in the current review were first divided into three categories, namely simple predictors, mediators, and moderators. These were defined as follows:

1. A *simple* predictor variable is one that is measured at baseline, and that directly predicts change in the outcome variable over time.
2. A treatment *mediator* identifies possible mechanisms through which treatment impacts on outcome (Kraemer, Wilson, Fairburn, & Agras, 2002), and should be defined as a measure of an event or change that occurs *after* the onset of treatment (Wilson, Fairburn, Agras, Walsh, & Kraemer, 2002). This can be either a change in the level of a baseline variable early in the course of treatment (for example, change in baseline depression during treatment could affect outcome) or change in another variable (for example, baseline depression could lead to increased anxiety during treatment, thus affecting outcome). Operationally, one would document temporal precedence (with the independent variable preceding the mediator), correlation between these two variables, and when one considered the two variables jointly, either total mediation or partial mediation (Kraemer et al., 2002).
3. Treatment *moderators* identify for whom and under what circumstances treatments have effects (Kraemer et al., 2002) i.e., variables that influence the strength or the direction of a relationship between a predictor variable and an outcome variable. By definition, a moderator is measured at pre-treatment and has no correlation with the treatment condition at baseline. Apart from an interaction between the moderator and predictor variable predicting outcome, a main effect between the moderator and the outcome may also exist. Moderators are often studied in terms of their relationship with treatment type, i.e. to determine whether a baseline characteristic makes a particular type of treatment more or less beneficial.

Following this grouping by relationship with outcome, predictors that were examined in at least three studies were grouped by category (e.g., eating disorder

behaviours, personality disorders). Predictors that appeared in only one or two studies were grouped in a residual category termed 'miscellaneous predictors'. The full table including predictors not included in the meta-analysis is available on request from the first author**.**

2.3.6 Grouping effects for the meta-analysis.

In some cases, multiple effect sizes from the same study were calculated. This was to indicate where a single predictor was used to predict more than one type of outcome (e.g., BMI and quality of life), or where an outcome was measured at more than one time point (e.g., at end of treatment and at 12 month follow-up). It is not recommended to include multiple effects from a single study in the meta-analytic process, as this increases the risk of a single study biasing the results (Brewin, Kleiner, Vasterling, & Field, 2007). In order to mitigate the influence of such biases, all effects were first divided into those measuring outcome at the end of treatment (EoT), and those measuring outcome at a post-treatment follow-up. Next, for studies where multiple effects were present for a single predictor or outcome, these effects were combined into a single effect size. For example, if separate effect sizes were given for distinct outcomes measures (e.g., BMI and ED pathology), these were amalgamated. Similarly, if a study measured an outcome at both 6- and 12-month follow-up, these two effects were combined into a single follow-up effect size. The final study groupings used in the analyses is given in **Table 1.**

2.3.7 Statistical analysis.

Effect sizes. For each outcome variable, an effect size expressed as the correlation coefficient, *r*, was calculated, where r = .10 constitutes a small effect, r = .30 a medium effect, and r = .50 a large effect (Cohen, 1992). Correlation coefficients were chosen as the effect size metric because they have been shown to best enable interpretation of the practical importance of an effect (Field, 2001). The *r* statistic was obtained by entering the reported statistical outcomes into an effect size calculator (Wilson, 2014). Studies were only included in the meta-analyses if the authors provided sufficient statistics such that an

effect size could be calculated. Effect sizes were calculated for both significant and non-significant findings.

Publication biases. In order to assess the effect of the so-called 'file drawer problem' of unpublished, non-significant or missing studies, the 'fail safe N' was calculated for each meta-analysis conducted. The fail safe N provides an estimate of the number of such studies that would need to be added to the meta-analysis to reduce an overall effect size to a non-significant level (Rosenberg, 2005). When the fail safe number is greater than the number of studies included in the meta-analysis, there is a greater likelihood that the observed meta-analytic effect size is robust to the file drawer problem. The problem of not reporting of non-significant results is also minimized in this type of study as authors tended to examine multiple predictors of outcome and reported by significant and non-significant findings.

***Method of meta-analysis*.** In order to be considered in a meta-analysis, the predictor variable was required to have featured in at least 3 different studies. Based on recommendations from Field and Gillett (2010), a random-effects model was used, as this type of model is considered appropriate to enable inferences to generalize beyond just those studies included in the meta-analysis. We used the Hedges and Vevea method of meta-analysis (Hedges & Vevea, 1998), in which effect sizes are first converted into a standard *z* metric before the average of the scores is calculated. Importantly, this method also has the advantage that it weights each effect based on study sample sizes.

2.4 Results

The results of the search strategy are shown in **Figure 2.1.** There were 147 studies that met criteria for inclusion in the qualitative synthesis. Inclusion criteria for the meta-analysis was met by 126 studies (86%), in that they examined at least one predictor for which there were sufficient data reported to calculate an effect size, and the predictor was also examined in at least two other studies. Due to the length of the summary of the 126 studies, the table is not reproduced within the main body of the chapter, but can be found

in the published version of the manuscript (Vall & Wade, 2015a). The results of the meta-analysis with the overall weighted effect size for each sub-group of predictors is given in **Table 2.1.**

2.4.1 Simple predictors of drop-out and outcome.

***Weight suppression*.** Greater weight suppression had only a small effect for treatment drop-out (mean r = .19), and a very small effect for EoT outcomes (mean r = .07). Moreover, although higher weight suppression predicted faster weight gain in a study of individuals with AN (Wildes & Marcus, 2012), it also predicted more binge/purge episodes.

***Binge/purge behaviours and driven exercise*.** More frequent binge/purge behaviours at baseline predicted worse outcome at both EoT (mean r = .22) and follow up (mean r = .19), and drop-out (mean r = .27). For individuals with AN, having the binge/purge subtype also predicted drop-out (mean r = .20). Lower levels of driven exercise was also predictive of good outcomes across EoT and 6-month follow-up (mean r = .40).

Motivation to recover. Individuals who felt more motivated and ready to change had better outcomes at EoT (mean r = .26) and at follow-up, albeit with a smaller effect size (mean r = .15). Motivation also predicted drop-out (mean r = .23), with less motivated individuals being more likely to be non-completers. Interestingly, it did not appear to matter how motivation was measured. In the articles reviewed, measures of motivation used in across studies varied considerably, from a single question assessed on a 10-point Likert scale which asked 'How ready are you to change your eating and weight?'(Bewell & Carter, 2008), to more lengthy measures such as the Anorexia Nervosa or Bulimia Nervosa Stages of Change Questionnaire (Castro-Fornieles et al., 2011; Wade, Frayne, Edwards, Robertson, & Gilchrist, 2009). In addition to baseline measures of motivation for recovery, a patient's motivation later in treatment may also predict longer term outcomes.

For example, motivation to recover later in treatment (specifically 4 weeks into treatment and at discharge) predicted the likelihood of relapse at 12 months better than motivation at admission (Carter et al., 2012). Also related to motivation, but not included in this analysis as not directly comparable with the other measures of motivation, in two guided self-help treatment programs for BN, greater compliance with the self-help materials was found to predict a greater likelihood of remission at 8 weeks (Troop et al., 1996) and greater abstinence from bulimic behaviours at 43 weeks post-completion (Thiels, Schmidt, Troop, Treasure, & Garthe, 2001). Also related to motivation but not included in the meta-analysis, self-efficacy (defined as one's confidence in their ability to change) was also a significant predictor of outcome in several studies. In a study of patients receiving guided self-help treatment for BN, higher self-efficacy emerged as the most robust predictor of better treatment outcome (Steele, Bergin, & Wade, 2011). Higher self-efficacy also predicted more favourable treatment outcomes in a study of underweight eating disorder patients (Pinto, Heinberg, Coughlin, Fava, & Guarda, 2008), and in a study of 484 severely underweight AN patients, those with higher self-efficacy had better outcomes at 2 year follow up, but not at 13-year follow-up (Rigaud, Pennacchio, Bizeul, Reveillard, & Vergès, 2011).

Global eating disorder pathology. Global eating disorder pathology was measured variously across studies by commonly utilised assessments such as the Eating Disorder Examination (Fairburn & Beglin, 1994) and the Eating Disorder Inventory (Garner, 1991). Lower levels of global eating disorder pathology at baseline predicted a better outcome for both AN and BN across a number of studies. At end of treatment, the mean effect of global eating disorder pathology on outcome was small (mean $r = .23$). Although this increased overall at follow-up (mean $r = .37$), this effect was not significant due to the large degree of variation in the effects reported across the three included studies ($r = .04$ to $r = .86$).

BMI. A higher BMI predicted a better outcome at both EoT (mean *r* = .36) and follow up (mean *r* = .24). With the exception of two studies of individuals with BN, all of the studies examined individuals with AN.

Depression. Lower depression predicted better outcomes at EoT (mean *r* = .23) and with a smaller effect size at follow-up (mean *r* = .19).

Self-esteem. Higher self-esteem predicted better outcomes at follow-up (mean *r* = .31), but not at EoT (mean *r* = .22), due to the large differences in the effects reported across the three included studies (*r* = .05 to *r* = .57).

Weight and shape concern. Lower weight/shape concern predicted better outcomes at EoT (mean *r* = .25). This effect remained but with a smaller magnitude in the meta-analysis of studies examining follow-up outcomes (mean *r* = .16).

General psychopathology. Lower comorbid psychopathology predicted better outcomes at EoT (mean *r* = .25). Although this effect was maintained overall at follow-up (mean *r* = .26), it was not significant due to the large differences in the effects reported across the three included studies (mean *r* = .02 to *r* = .61).

Age of onset/illness duration. Individuals who had an older age of onset or a shorter illness duration generally had better outcomes at EoT with small effect size (mean *r* = .19). This effect was of a similar magnitude at follow-up (mean *r* = .16).

Interpersonal relationships.

Interpersonal functioning. Better interpersonal functioning at baseline predicted outcome at both EoT (mean r = .21) and follow up (mean r = .27). The individual effects were generally larger in studies of individuals with BN and BED compared to those with AN.

Familial problems. More problems in the family environment predicted worse outcomes both at EoT (mean *r* = .36) and follow up (mean *r* = .36). Four of the seven studies examined were of adolescent patients. No BED studies met inclusion for this

category. It should also be noted that the studies included in this category employed different predictor measures (e.g., parental depression, parental substance abuse), and although they all indicate greater problems in the family environment, caution should be taken when interpreting this finding.

2.4.2 Interactive simple predictors of treatment outcome.

Several studies have also identified moderators of outcome that are not based on treatment type but there were insufficient numbers of such studies to include in a meta-analysis. Baseline self-compassion and fear of self-compassion interacted to predict changes in eating disorder symptoms over time for individuals being treated in specialized eating disorder programs (Kelly, Carter, & Borairi, 2014). Specifically, poorer outcomes we observed for patients who were both fearful of, and low in, self-compassion, e.g., patients who were low in self-compassion only experienced a poor outcome if they were also fearful of self-compassion, and vice versa. For individuals with BED, greater concerns about shape and weight were predictive of non-response at the end of treatment among those patients with low interpersonal problems (Hilbert et al., 2007). In women with AN treated in a day hospital program, AN subtype moderated the relationship between attachment style and drop-out (Tasca, Taylor, Ritchie, & Balfour, 2004). Those with avoidant attachment were more likely to drop-out from treatment, but only if they were of the binge/purge subtype, while those with an anxious attachment style were more likely to complete treatment, but only if they were binge/purge subtype. Finally, for individuals with AN receiving inpatient treatment, BMI moderated the relationship between weight suppression and outcome. For individuals with lower admission BMIs, greater weight suppression predicted better discharge outcome, while for those with higher admission BMIs, greater weight suppression predicted unfavourable discharge outcomes (Berner, Shaw, Witt, & Lowe, 2013).

2.4.3 Mediators.

Early symptom improvement. A mediational process that emerged as a significant predictor of outcome with a medium to large effect size, is the rate at which, and extent to, eating disorder symptoms responded to treatment. Patients who responded more quickly or more robustly, particularly in the early stages of treatment, had better outcomes at EoT (mean r = .51) and follow up (mean r = .35). Although not included in the meta-analysis as not directly comparable to other the outcome definitions in the included studies, change in body image during treatment accounted for a large proportion of change in eating disorder pathology for inpatients being treated for all eating disorders (Danielsen & Rø, 2012). However, this change only predicted change in patient scores on the Eating Disorder Inventory (EDI), but not change in BMI.

As well as weight gain predicting a better response for individuals with AN, weight loss early in treatment is likely to indicate a worse outcome. Individuals with AN treated as inpatients who lost weight in weeks 3 or 4 of treatment were much less likely to gain the minimum expected weight by discharge (Hartmann, Wirth, & Zeeck, 2007).

***BMI at discharge*.** Another mediational predictor of outcome with small-medium effect size was a patient's BMI at discharge. All studies included in the meta-analysis were of patients with AN. Results indicated that patients who had a higher weight at discharge had better outcomes at follow up (mean r = .29). Studies included both inpatient and outpatient samples and included follow-up periods from 12 months to 4.6 years. Interestingly, the two studies with the greatest effect size were those that examined a longer follow-up period, suggesting that discharge BMI may be a better predictor of long-term outcome.

***Miscellaneous mediational predictors*.** As the following mediators were not examined in at least 3 studies, no meta-analysis of these effects was undertaken. The following results provide a narrative description of these novel mediational predictors. In adults with either AN or BN, a greater reduction in shame (in regards to their body,

character, and behaviour) during the first 4 weeks of treatment lead to faster rate of improvement in eating disorder symptoms over 12 weeks of treatment (r = .23) (Kelly et al., 2014). In the same study, an early increase in self-compassion led to greater reductions in shame over 12 weeks (r = .15). A novel mediational finding in a recent study suggested that changes in parent self-efficacy during the course of family based treatment predicted adolescents' treatment outcome in a sample of 49 adolescents with AN or BN (Robinson, Strahan, Girz, Wilson, & Boachie, 2013). Specifically, parents who exhibited a greater increase in self-efficacy had children who subsequently reported the greatest improvements in eating disorder symptoms, depression and anxiety, both at 3 and 6-month follow-up, with effect sizes ranging from r = .26 to r = .51.

2.4.4 Moderators of treatment type.

As no moderators were examined in at least 3 studies, no meta-analysis of moderator effects was undertaken, so a narrative description is instead provided. In adolescents receiving treatment for BN, the severity of eating disorder psychopathology was found to moderate the relationship between treatment type and outcome (Le Grange, Crosby, & Lock, 2008). Specifically, participants who received family-based therapy were more likely to meet criteria for partial remission at follow-up compared to those receiving individual treatment, but only if they exhibited more severe eating disorder psychopathology (r = .22). In a similar study of adolescents with AN receiving either short or long term family-based therapy (Lock, Agras, Bryson, & Kraemer, 2005), two moderators of treatment outcome were identified. The first was eating related obsessionality. Specifically, a longer course of therapy was found to be better than a shorter course of therapy, but only for those individuals with high levels of eating related obsessionality (r = .29). The second was family structure. Individuals with non-intact families (single parent, divorced) did better with longer treatment than shorter treatment (r = .31). For adolescents receiving either family-based therapy or individual, adolescent-

based therapy for AN (Le Grange et al., 2012), eating related obsessionality and severity of eating disorder psychopathology both moderated outcome (r = .23 and r = .32 respectively). Specifically, individuals with higher levels of these variables had better outcomes in the family therapy, compared to the individual therapy. In a comparative study of Cognitive Behaviour Therapy (CBT) versus medication treatments (fluoxetine) for individuals with BED (Grilo, Masheb, & Crosby, 2012), over-evaluation of weight and shape significantly moderated the relationship between treatment received and outcome. Specifically, participants with higher overvaluation had significantly greater reductions in eating disorder psychopathology and depression levels if receiving CBT compared to those receiving medication only. There was insufficient data reported to calculate effect sizes for these findings.

In adults with AN, baseline set-shifting was found to moderate outcome, such that those with poor baseline set-shifting benefited more from cognitive remediation therapy than from treatment as usual (r = .18) (Dingemans et al., 2013). However, this finding was only in regards to the quality of life outcome measure, and did not extend to the general eating disorder pathology outcome.

Finally, a number of moderators were reported in a trial comparing CBT-AN and specialist supportive clinical management (SSCM) in adults with severe and enduring AN (Le Grange, Fitzsimmons-Craft, et al., 2014). Outcomes were eating disorder related quality of life, general mental health and depressive symptoms. No moderators were found for the quality of life outcomes. However, with respect of the general mental health outcome, having an older age, more severe eating disorder psychopathology or depression made one more likely to benefit from CBT-AN compared to SSCM. For the depressive symptoms outcome, having binge/purge subtype of AN or more severe eating disorder psychopathology made one more likely to benefit from CBT-AN. Effect sizes ranged from r = .25 to r = .30.

2.5 Discussion

The purpose of this systematic review and meta-analysis was to identify and quantify the predictive value of variables associated with outcome for individuals who received treatment for an eating disorder.

2.5.1 Implications for treatment.

Aim to achieve symptom reduction early in treatment. Investing a greater effort in ensuring that patients achieve greater symptom reduction in the early stages of treatment appears to be an important goal for achieving better treatment response. Additionally, given that failure to respond early to treatment may also be a risk factor for less favourable outcomes in the longer term (McFarlane, Olmsted, & Trottier, 2008; Raykos, Watson, Fursland, Byrne, & Nathan, 2013), identifying those individuals who fail to respond early in treatment could help to ensure that more intensive follow-up and intervention is conducted where appropriate.

Identify individuals with severe eating disorder pathology early in treatment. Routinely assessing pathology at admission will help to identify patients with more severe symptoms, across binge/purge symptoms, depression, ED psychopathology, BMI (for AN), duration of disorder, driven exercise, and weight and shape concerns. Individuals with more severe problems in these areas are likely to have worse outcomes, and may be at greater risk of dropping-out of treatment (Hubert et al., 2013). Such assessments may assist clinicians to put in place safe-guards to encourage retention, including discussing these issues openly with the client. The finding that low levels of self-compassion and fear of the consequences of being self-compassionate decrease the benefit obtained from therapy (Kelly, Carter, Zuroff, & Borairi, 2013) allied with the finding that higher levels of perfectionism and self-criticism are associated with higher levels of psychopathology and comorbidity (Egan, Wade, & Shafran, 2011), may indicate that an early focus on self-compassion with this group may be of benefit. Ensuring that patients with severe pathology are not discharged from treatment before they have reached a satisfactory level of

improvement may also assist in achieving better long-term outcomes (Brewerton & Costin, 2011; Kaplan et al., 2009).

Focus on motivation and confidence to change at all points in treatment. Patients who entered treatment with higher motivation and self-efficacy had a more favourable outcome. This suggests that increasing motivation may be a potential strategy to improve treatment efficacy. Although attempts have been made to heighten motivation through motivational interviewing in several treatment studies, their success has been mixed. One review of motivational interviewing as an addition to eating disorder treatment concluded that it may be a promising addition to other therapy, particularly in the early stages of treatment (Macdonald, Hibbs, Corfield, & Treasure, 2012), but other reviews have concluded that there is little evidence to support the efficacy of this technique (Dray & Wade, 2012; Knowles, Anokhina, & Serpell, 2013). Given that higher self-efficacy was also identified as a predictor of better outcomes across several studies, one possibility is that interventions need to focus more on a person's confidence in their *ability* to change. Waller (2012) has suggested that it is actual behavioural change that matters most with respect to motivation in eating disorder treatment. Consistent with the studies that show early symptom change to be predictive of good outcome, an early focus on manageable behavioural experiments may be an important focus of therapy. In addition, focus on motivational enhancement appears to be important not only at treatment commencement, but also when a patient has already begun treatment and experienced the benefits of this change (Carter et al., 2012; Wade et al., 2009).

2.5.2 Limitations of current research and recommendations for future research.

Although this review identified several factors that were indicated across studies as being important for treatment response, there are still significant gaps and inconsistencies in the body of literature that limit the extent to which robust conclusions can be drawn. A

good degree of consistency and replication is needed before the field can confidently decide that changes in clinical practice and treatment approaches are warranted. In order to advance this area and enhance the ability to predict patient outcomes, it will be necessary to address the following limitations.

Predictors across diagnoses and treatment type. Although this area continues to grow, the analysis of predictors by specific diagnosis or treatment type is currently limited by the small number of studies in each category. As such, we were unable to conduct analyses of each predictor by eating disorder subtype or by specific treatment type. Instead, to allow for more robust statistical analyses to be conducted, we have attempted in this review to provide a preliminary overview of predictors across subtypes and treatment types. This approach necessarily requires a heterogeneous inclusion of studies, and as such the conclusions about the predictive value of variables for specific populations must be interpreted with this limitation in mind. Relatedly, there are many confounding variables that may moderate predictor-outcome associations that were not examined, such as treatment duration, follow-up duration, study population (inpatient/outpatient), primary study quality, and inclusion of measures of variable psychometrics. As this body of research grows, so too will the ability to conduct more targeted analyses to answer specific questions about predictors of outcomes for specific populations and across specific treatment modalities.

Disparate definitions of treatment outcome. Across the studies examined in the present review, measures of outcome variously included rate of weight gain, achievement of full remission, length of stay and rate of relapse. This is problematic, because when comparing treatment studies, such differences make comparison of the overall outcomes, and of any predictors of outcomes, extremely difficult (Williams, Watts, & Wade, 2012). Several studies highlight the problems of disparate outcome definitions. One study applied a range of definitions of remission to a single dataset, and found that remission rates

ranged between 30% and 44% for BN, and 20% and 59% for eating disorders not otherwise specified (EDNOS), depending on the definition used (Björk, Clinton, & Norring, 2011). In adolescents with AN, rate of recovery was calculated using either percent ideal body weight, psychological recovery, or combinations of these variables. Depending on the definition used, recovery rates varied from 57.1% to 94.4% (Couturier & Lock, 2006). Different definitions of relapse and remission were applied to adult women with BN followed up for 19 months, and depending on the definition used, relapse rates ranged from 21% to 55% (Olmsted, Kaplan, & Rockert, 2005).

Like treatment outcome, treatment completion has been disparately defined in the literature (Fassino et al., 2009). In this review, drop-out was defined in one study as patient initiated termination of treatment without the sanction of the treatment team, while in another study patients who did not fulfil the therapeutic contract (i.e. did not reach the goal discharge weight) were classified as dropping out.

It will be necessary for researches to adopt shared and consistent definitions of outcome. One such approach is described by Bardone-Cone and colleagues (Bardone-Cone et al., 2010), who examined definitions of recovery used in the eating disorder literature by applying the definitions to the same dataset and suggested that full recovery be defined as a combination of: (i) no longer meeting criteria for an eating disorder, (ii) abstinence from bingeing, purging and fasting for 3 months, (iii) body mass index $\geq$ 18.5, and (iv) EDE or EDE-Questionnaire (EDE-Q) subscale scores all within 1 SD of healthy, age-matched population norms. Using this definition, which has the advantage of transdiagnostic application, participants with either AN, BN, or EDNOS who met criteria for full recovery were indistinguishable from healthy controls on measures of several eating disordered related cognitions. A recent review compared seven commonly employed definitions of remission in women with AN, BN or EDNOS (Ackard, Richter, Egan, & Cronemeyer,

2014). The Bardone-Cone definition was found to be the most robust, as well as the most consistent across diagnoses.

As well as adopting shared definitions of outcomes, researchers will also need to consider the timing at which outcome is measured. In this review, outcome was measured during treatment, at end of treatment, several months post-treatment, up to a number of years after treatment completion. There is growing evidence that early changes during treatment (Doyle, Le Grange, Loeb, Doyle, & Crosby, 2010; Lock, Couturier, Bryson, & Agras, 2006; McFarlane et al., 2008; Raykos et al., 2013) and outcomes immediately post-treatment (Bean et al., 2004; Brewerton & Costin, 2011; Kaplan et al., 2009; Lock & Litt, 2003) are important for longer-term recovery and symptom improvement. However, more research is needed to examine the question of timing, and firm conclusions about predictors needs to consider the fact that a predictor may be significant at one time point, but not another.

The question of defining drop-out is similarly complex. More rigour is needed around the reporting of who initiates drop-out, and the time-point at which it occurs. In addition, a recent review of dropout from outpatient treatment for AN noted a number of flaws in the way that drop-out is reported (DeJong, Broadbent, & Schmidt, 2012), and suggests a framework for reporting on drop-out from eating disorder treatment.

Inclusion of effect sizes. Fourteen percent of eligible studies were excluded from the current meta-analysis because insufficient data was included in many studies to allow the calculation of effect sizes for examined variables. In particular, data regarding findings that were not statistically significant were frequently omitted. A recommendation for future studies is that such data are included in publications to enable comparison of effects across studies.

Second, it is recommended that as well as reporting outcome data, studies also report effect sizes, particularly to accompany statistically significant findings. When

statistically significant findings were converted to an effect size for the purpose of the current meta-analysis, the magnitude of many of these findings was of very limited practical significance. By contrast, the effect sizes associated with some of the non-significant findings was comparable (or greater) in magnitude than many of the significant findings. The need to place a greater emphasis on the importance of results, rather than just statistical significant, has been argued for some time, such as by Ioannidis (2005), and there has been renewed interest in this matter recently. At least one prominent journal has recently added to its publishing policy the inclusion of effect sizes (Eich, 2014) and published a detailed user guide (Cumming, 2014) to assist authors in this endeavour.

Limited transdiagnostic findings. Although eating disorders are increasingly being conceptualised (and treated) transdiagnostically (Dalle Grave et al., 2013; Fairburn et al., 2003; Wade et al., 2006), the trend in the literature is still to deal with them categorically, as separate conditions. As a result, the predictor variables identified were generally applicable to either AN, BN or BED, but rarely to all. Where a variable could be identified as predicting outcome across all the eating disorder subtypes, this was often based on separate studies which employed different methodologies and different outcome measures, limiting the confidence with which conclusions about the robustness of a predictor across conditions can be drawn. As described above, this makes comparison of findings across studies difficult and limits the generalisability of findings. Future studies should attempt, where possible, to examine predictor variables across the full eating disorder spectrum, which will be enabled by the definition of outcome suggested in the current study.

Continuing to examine complex predictor models. Encouragingly, an increasing number of mediational and moderational analyses are beginning to appear in the predictor literature. There are several important potential applications of such research. Mediational models are providing insight into which processes should be monitored during treatment, and which changes we should be striving for in order to achieve the best patient outcomes.

Moderational analyses are beginning to help answer questions about which patients would benefit most from which treatments. Although more studies are needed to replicate and extend such findings, being able to allocate patients to the treatment most likely to be effective for them, rather than simply trial and error, could save considerable time and resources. It is recommended that future studies attempt to identify processes that involve moderation and mediation when analysing predictor variables. This echoes calls to consider moderational and mediational processes in all eating disorder intervention studies (Agras et al., 2004). In particular, care should be taken to correctly define the mechanisms of interest and to use appropriate statistical techniques in these analyses. Kraemer and colleagues (2001) have provided comprehensive guidelines to assist researchers with such tasks.

Neurocognitive functioning. Neuropsychological studies have repeatedly highlighted deficits in cognitive flexibility (particularly impaired set-shifting) in individuals with AN (Treasure & Schmidt, 2013) and BN (Roberts, Tchanturia, & Treasure, 2010). There is also some evidence that these deficits may be related to treatment response. For example, functional magnetic resonance imaging was used to examine the performance of individuals with and without AN on a theory of mind (ToM) task (Schulte Ruther, 2012). Individuals with AN displayed deficits in those brain areas associated with ToM, and these deficits were associated with a poor clinical outcome at 1-year follow-up. Including neurocognitive tasks in future studies, particularly those that measure processes that are thought to be important in eating disorder pathology (for example, set-shifting), could provide important insights into treatment response and potential novel interventions.

Genes and environment. A further area to consider in future research on the prediction of treatment outcome is interactions between genes and the environment (GxE) in terms of impact on treatment. Research to date clearly indicates a role of additive genetic action in the pathogenesis of eating disorders (Trace, Baker, Peñas-Lledó, & Bulik,

2013), with a focus to date on interactions involving the 5-HT transporter promoter *5-HTTLPR* and the relation to severity of the expressed eating disorder. Increased psychopathology has been indicated in an interaction between the *5-HTTLPR* short allele and childhood maltreatment in bulimia nervosa (Steiger et al., 2007; Steiger et al., 2008; Steiger et al., 2009) and increased vulnerability to anorexia nervosa has been indicated by an interaction between the *5-HTTLPR* short allele and problematic parenting style (Karwautz et al., 2010). It is conceivable that more adverse environments in conjunction with specific genetic expression can impede ability to receive benefit from therapy for eating disorders. A relationship between genes and treatment response has been demonstrated in other clinical populations. For example, in a sample of individuals with post-traumatic stress disorder (PTSD), individuals in the 5-HTTLPR low-expression genotype group (S or LG allele carriers) were likely to respond poorly to CBT treatment. Specifically, this group exhibited more severe PTSD symptoms at 6-month follow-up compared to patients who did not fit this genotype (Bryant et al., 2010).

2.6 Conclusion

The identification of predictors, moderators and mediators of outcome is an important goal in the quest for improving outcomes in eating disorder treatment. Encouragingly, an increasing number of treatment studies are investigating this question in their analyses. This growing body of literature has begun to highlight consistent baseline predictors of treatment outcome, including motivation and self-efficacy, weight and shape concerns, and binge/purge behaviours. Treatment moderators and mediators are also beginning to receive more attention, and rate of symptom change during treatment in particular has been shown across numerous studies to have predictive value. Further consolidation of these foundations is now necessary in order to inform the modification and development of effective clinical interventions such as individualised treatment approaches. In particular, studies should adopt shared and robust definitions of outcome, and seek to examine predictors of outcome across the full spectrum of eating disorder

subtypes. A focus on emerging areas such as neurological and genetic bases of eating disorders may also provide important insights for the ongoing advancement of eating disorder treatment.

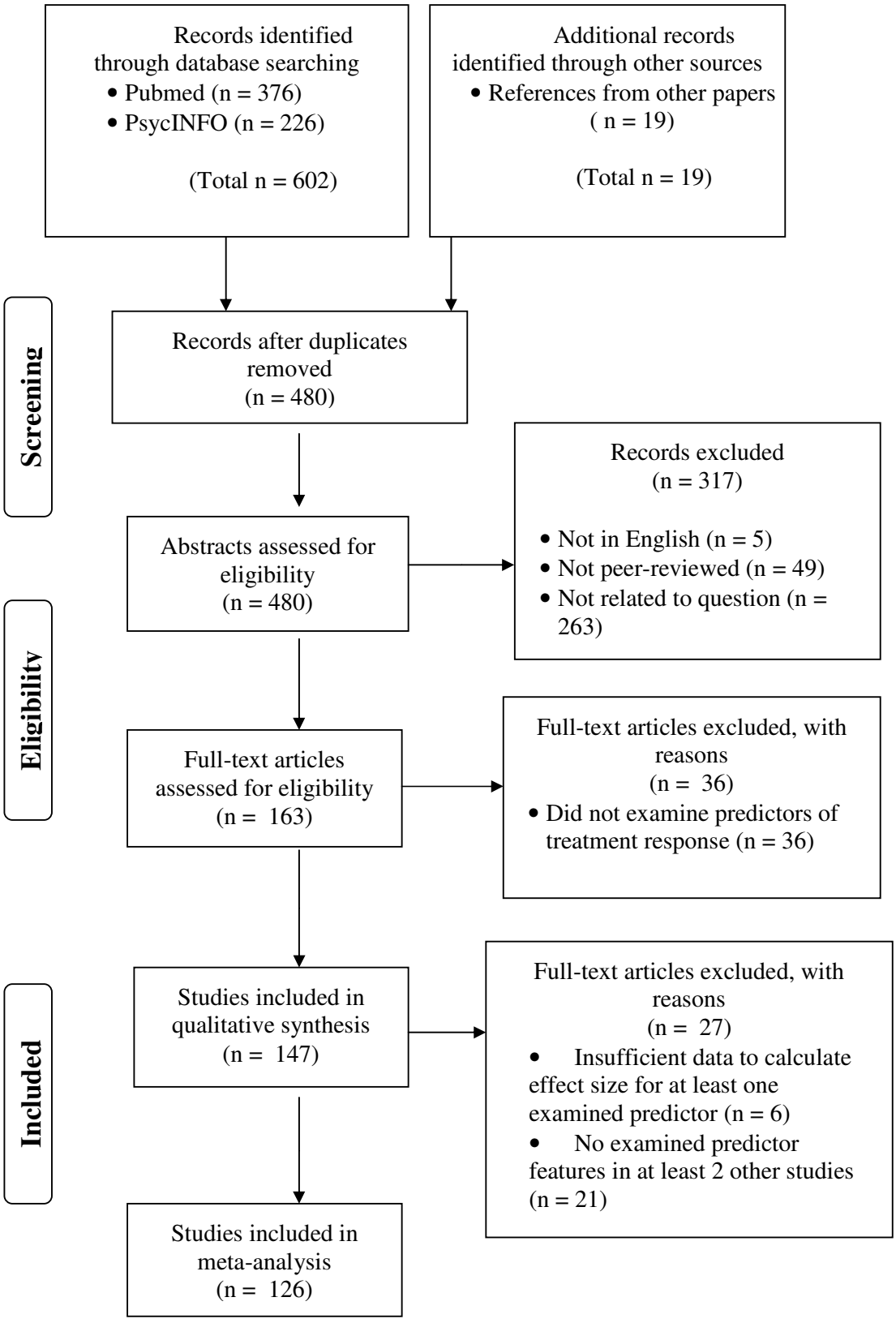

Figure 2.1 PRISMA flow diagram of study selection.

Table 2.1

Results of meta-analysis for each predictor variable

Simple predictors of drop-out									
	k	***Mean r***	***Variance***	***95% CI***	***Z***	***p***	***Q***	***p***	***Failsafe N***
Higher weight suppression	6	.19	.094	-.07:.42	1.46	.145	4.12	.532	53
Higher binge/purge frequency	3	.27	.007	.18:.37	5.39	<.001	.13	.940	27
Having binge/purge AN subtype	9	.20	.006	.13:.27	5.21	<.001	8.47	.389	154
Lower motivation	5	.23	.005	.13:.32	4.58	<.001	2.83	.587	36
Higher impulsivity	3	.19	.009	.12:.27	5.11	<.001	1.70	.427	27
Greater comorbid psychopathology	4	.16	.004	.07:.25	3.46	.001	1.90	.593	11
Greater depressive symptoms	3	.18	.148	-.28:.56	0.75	.451	1.78	.411	0
Simple predictors of better outcome at EoT									
	k	***Mean r***	***Variance***	***95% CI***	***Z***	***p***	***Q***	***p***	***Failsafe N***
Lower ED pathology	7	.23	.024	.09:.37	3.15	.002	5.50	.481	66
Lower binge/purge frequency	1	.22	.016	.12:.31	4.51	<.001	10.03	.528	263
Higher BMI	6	.36	.089	.11:.56	2.81	.005	5.01	.415	121
Greater motivation to recover	9	.26	.003	.18:.33	6.66	<.001	5.88	.660	133
Lower depression	9	.23	.017	.10:.34	3.55	<.001	8.11	.426	68
Higher self-esteem	3	.22	.037	-.40:.45	1.66	.097	2.92	.232	8
Lower shape/weight concern	5	.25	.002	.17:.33	5.97	<.001	3.96	.411	82
Better interpersonal functioning	5	.21	.005	.14:.28	5.56	<.001	1.27	.866	52
Lower comorbid psychopathology	4	.25	.002	.16:.33	5.54	<.001	2.64	.451	34
Shorter duration/lower onset age	7	.19	.005	.10:.28	3.92	<.001	6.20	.402	54
Lower weight suppression	6	.07	.001	.00:.13	2.02	.043	3.06	.690	2
Less exercise*	4	.40	.003	.31:.49	8.13	<.001	2.00	.573	92
Fewer familial problems	4	.36	.069	.23:.49	4.96	<.001	2.99	.393	49

Note: *k* = number of studies, Q = *Q*-statistic for homogeneity of variances assumption, Z = *Z*-value for two-tailed test of null

Table 2.1 (continued).

Results of meta-analysis for each predictor variable

Simple predictors of better outcome at follow-up									
	k	***Mean r***	***Variance***	***95% CI***	***Z***	***p***	***Q***	***p***	***Failsafe N***
Lower ED pathology	5	.37	.580	-.28:.79	.23	.261	1.91	.752	389
Lower binge/purge frequency	1	.19	.006	.13:.25	.11	<.001	17.09	.380	361
Higher BMI	1	.24	.020	.14:.34	.44	.001	10.18	.425	231
Greater motivation to recover	6	.15	.007	.06:.24	.38	.001	3.28	.656	20
Lower depression	6	.19	.003	.09:.28	.71	<.001	4.26	.513	21
Higher self-esteem	3	.31	.034	.05:.53	.36	.018	2.38	.305	13
Lower shape/weight concern	3	.16	.012	.00:.31	.98	.048	2.34	.310	7
Better interpersonal functioning	4	.27	.005	.17:.36	.13	<.001	2.08	.361	33
Lower comorbid psychopathology	4	.26	.117	-.08:.55	.49	.137	2.57	.464	39
Absence of personality disorders	6	.13	.002	.06:.19	.74	<.001	4.21	.520	25
Shorter duration/lower onset age	1	.16	.008	.09:.23	.48	<.001	4.81	.851	59
Fewer familial problems	4	.36	.035	.16:.53	.41	<.001	2.48	.479	62
Mediators of better outcome at EoT									
	k	***Mean r***	***Variance***	***95% CI***	***Z***	***p***	***Q***	***p***	***Failsafe N***
Early symptom change	1	.51	.044	.40:.61	.04	<.001	14.25	.219	1207
Mediators of better outcome at follow-up									
	k	***Mean r***	***Variance***	***95% CI***	***Z***	***p***	***Q***	***p***	***Failsafe N***
Early symptom change	7	.35	.008	.26:.45	.65	<.001	7.15	.307	195
Discharge BMI	6	.29	.050	.09:.47	.82	.005	4.15	.528	69

Note: *k* = number of studies, Q = *Q*-statistic for homogeneity of variances assumption, Z = *Z*-value for two-tailed test of null.

Chapter 3

Trail Making Task Performance in Inpatients with Anorexia Nervosa and Bulimia Nervosa[2]

[2] Material from this chapter has been published in the *European Eating Disorders Review* [Vall, E., & Wade, T. D. (2015). Trail making task performance in inpatients with anorexia nervosa and bulimia nervosa. *European Eating Disorders Review, 23*, 304-311.]

3.1 Abstract

Objective: Set-shifting inefficiencies have been consistently identified in adults with anorexia nervosa (AN). It is less clear to what degree similar inefficiencies are present in those with bulimia nervosa (BN). It is also unknown whether perfectionism is related to set-shifting performance.

Method: We employed a commonly used set-shifting measure, the Trail Making Test (TMT) to compare the performance of inpatients with AN and BN with a healthy control sample. We also investigated whether perfectionism predicted TMT scores.

Results: Only the BN sample showed significantly sub-optimal performance, while the AN sample was indistinguishable from controls on all measures. There were no differences between the AN subtypes (restrictive or binge/purge), but group sizes were small. Higher personal standards perfectionism was associated with better TMT scores across groups. Higher concern over mistakes perfectionism predicted better accuracy in the BN sample.

Discussion: Further research into the set-shifting profile of individuals with BN or binge/purge behaviours is needed.

3.2 Introduction

Eating disorders are disabling mental conditions that are associated with significant impairment to functioning across physical, social, vocational and educational domains (Hay & Mond, 2005; Mond et al., 2004). Outcomes for patients with an eating disorder remain sub-optimal even after intensive intervention, with around 50 per cent retaining their diagnosis ten years after treatment (Keel & Brown, 2010). In an attempt to improve treatment approaches, there has been increasing interest in the identification of possible endophenotypes for eating disorders, with a view to developing etiological based models which may guide the development of novel treatment approaches (Bulik et al., 2007). One target in this line of enquiry is the rigid and inflexible style of executive functioning commonly seen in individuals with an eating disorder, which is considered as a risk factor for both development and maintenance of disordered eating in several prominent models of disordered eating (Fairburn et al., 2003; Schmidt & Treasure, 2006; Treasure & Schmidt, 2013). Problems with set-shifting, i.e., the ability to switch between tasks or mental sets in response to changing goals or environmental stimuli (Tchanturia et al., 2012; Tchanturia et al., 2011), have been consistently identified in individuals with anorexia nervosa (AN) (Abbate-Daga, Buzzichelli, Marzola, Amianto, & Fassino, 2014; Holliday, Tchanturia, Landau, Collier, & Treasure, 2005). Set-shifting inefficiencies have been demonstrated across all phases of the illness, including those in acute stage and those who are recovered (Danner et al., 2012; Roberts et al., 2010; Tenconi et al., 2010). A recent systematic review and meta-analysis of studies examining set-shifting in adolescents with AN (Lang, Stahl, Espie, Treasure, & Tchanturia, 2014) found that adolescents generally showed less problems with set-shifting compared to adults with AN, and another study found that poorer performance was associated with a longer duration of disorder rather than a specific type of disorder (Roberts et al., 2010). This contradicts the notion that

poor set-shifting is an endophenotype of disordered eating, and might suggest that it is impacted by the chronicity of the illness.

There has been considerably less focus on set-shifting in individuals with bulimia nervosa (BN), and results have been conflicting, with only a handful of studies indicating differences between BN and control groups (Van den Eynde et al., 2011). However in one study, poor set-shifting was associated with binge-purge eating disorders (AN and BN) rather than malnutrition (Roberts et al., 2010). In another study, no differences were found between individuals with AN of the restrictive subtype (AN-R) and the binge-purge subtype (AN-BP) on set-shifting ability (Van Autreve, De Baene, Baeken, Heeringen, & Vervaet, 2013).

Another question that remains unanswered is whether this sub-optimal set-shifting performance is explained by perfectionism, which has been indicated as a key factor in the development and maintenance of disordered eating (Bardone-Cone et al., 2007; Jacobi, Hayward, de Zwaan, Kraemer, & Agras, 2004). Perfectionism in the eating disorders has been described as the "incessant demand for the highest possible standards of behaviour and external approval" (Halmi et al., 2000, p. 1799), manifested in rigid, stereotypic, ritualistic behaviours and beliefs (Jacobi et al., 2004). There are obvious parallels between perfectionism and set-shifting, particularly in the centrality of cognitive rigidity to both constructs. Indeed, the original Cognitive-Interpersonal Maintenance Model of AN (Schmidt & Treasure, 2006) considered perfectionism and cognitive rigidity together as risk and maintenance factors for the illness. Moreover, like problems with set-shifting, elevated perfectionism has been found to persist even after recovery from an eating disorder (Bardone-Cone et al., 2007), indicating that these may be stable trait markers rather than an effect of the ill-state. Despite the potential links between perfectionism and set-shifting, the relationship between the constructs has been little studied. In one study, individuals with AN who self-reported (retrospectively) higher

childhood perfectionism performed more slowly and made more errors on a trail making set-shifting task (Tchanturia et al., 2004). However, adult perfectionism and childhood and adult rigidity were not associated with set-shifting performance. In another study that compared women who had recovered from AN with a healthy control group, perfectionism (particularly concern over mistakes and personal standards) was associated with set-shifting, but with mixed results (Lindner, Fichter, & Quadflieg, 2014). In the recovered-AN group, higher personal standards and concern over mistakes were associated with fewer perseverative errors, but slower set-shifting time. By contrast, in the control group, higher perfectionism was associated with more perseverative errors but faster set-shifting. This might suggest that perfectionism is manifested differently in individuals with an eating disorder. For example, in the AN group, higher perfectionism might have rendered participants more fearful of making a mistake, and therefore likely to invest more time in the exercise to prevent this happening (resulting in a slower time, but fewer errors). On the other hand, perfectionism in the control group may have encouraged participants to perform faster, but without the associated fear of making a mistake, leading to faster times, but sacrificing accuracy.

One issue that may contribute to the variation noted in the set-shifting literature is the use of different tools of measurement of set-shifting. This is to be expected as any given test requires the deployment of a set of different functions, and it is good practise to use a variety of measures to gain a strong validated association. However, we also need to understand more about the validity of any given measure. One very commonly used measure is the Trail Making Test (TMT: Reitan, 1955), which in one systematic review was found to be the most commonly used test of set-shifting in the eating disorder literature (Roberts, Tchanturia, Stahl, Southgate, & Treasure, 2007). The TMT is attractive for its availability and simplicity to use, and has been shown to effectively measure visual search, motor speed, and mental flexibility

operations (Crowe, 1998). While the TMT was historically conducted as a pen and paper test, freely available electronic versions of the TMT have recently emerged. This advances the validity of the measure, given the reliance on timing in the TMT to generate set-shifting scores, pen and paper versions may be somewhat inaccurate. The wide availability of such a measure also enables means that research protocols can readily be replicated, allowing the comparison of findings across studies, and the potential for the establishment of robust normative data.

The aim of this study was therefore twofold. The first was to examine whether eating disorder subtype (particularly the presence of BN or binge/purge behaviours), would predict set-shifting performance as measured by a free, electronic version of the TMT. We hypothesised that in individuals with AN, those with AN-BP would have poorer set-shifting than those with AN-R, and that individuals with AN would perform worse compared to those with BN. The second aim was to examine the relationship between perfectionism and set-shifting, and specifically to investigate whether perfectionism would predict TMT scores across clinical and healthy control groups. We anticipated that higher perfectionism would be associated with worse set-shifting.

3.3 Method

3.3.1 Participants and procedure.

The project was approved by the Southern Adelaide Clinical Human Research Ethics Committee and the Flinders University Social and Behavioural Research Ethics Committee. Informed consent was obtained from all patients. In the clinical sample, consent was also obtained from the parents of patients under 18 years of age. Patients in the clinical samples were assessed within 48 hours of admission and completed the assessments on a laptop computer. The control sample was assessed at a laboratory in the School of Psychology, and also completed all assessments on a computer.

Participants in the clinical sample were consecutive, unique admissions to an adult inpatient hospital program at a public hospital (n = 53), in the 12 month period between August 2013 and September 2014. Briefly, the program specializes in the treatment of eating disorder patients who are medically stable. Patients must be at least 15 years of age and the study inclusion criteria required patients to be deemed to be medically fit for participation by the medical treatment team. Two participants were removed from the adult sample as they had extreme outlier scores on all eating disorder severity responses (defined as values greater than 1.5 times the interquartile range), thereby leaving 51 participants in the final sample. Although patients were not formally assessed for the presence of comorbid anxiety or depression, review of charts revealed that 41 (80.4%) had been prescribed, and that 40 (78.4%), were currently taking, some form of antidepressant medication.

The clinical sample consisted of both AN (n = 28) and BN (n = 23) cases. The AN group contained 18 cases that met the restrictive subtype and 9 who met the binge/purge subtype. One case did not meet the full DSM-5 criteria for AN as BMI was 19.3, which was above our threshold of 18.5, so was formally classified as OSFED-AN (restrictive subtype). Given the clinical presentation of this case and review of the patient's charts, this presentation was clearly consistent with AN-R subtype and was thus included in the AN-R group for subsequent analyses.

The control sample consisted of female undergraduate students who completed the study as part of their first-year psychology studies (n =181). One case was deleted as no data were recorded for the TMT. The sample was then screened to remove any cases with significant eating disorder pathology. People meeting full or partial criteria for an eating disorder were identified; 4 participants met the DSM-5 diagnostic criteria for BN and 25 met

the criteria for OSFED-BN. Two cases with extreme scores on the set-shifting variables were removed, leaving 149 normative cases (82.3% of the original sample).

3.3.2 Measures.

Eating disorder symptoms and severity. Behaviours and psychopathology were obtained using the Eating Disorder Examination – Questionnaire (EDE-Q: Fairburn & Beglin, 1994), which has been shown to possess good psychometric properties (Berg, Peterson, Frazier, & Crow, 2012)**.**

Eating disorder diagnosis. In the clinical sample, Diagnostic and Statistical Manual for Mental Disorders (DSM-5: APA, 2013) eating disorder diagnoses were made by the treating clinician (consultant psychiatrist or senior psychiatric registrar) at the initial admission assessment, and were confirmed by a multi-disciplinary team at weekly clinical review meetings. In the control sample, eating disorder diagnosis was determined via algorithms based on criteria from the DSM-5 using self-reported responses from the EDE-Q. These algorithms have been described in the literature (Quick, Berg, Bucchianeri, & Byrd-Bredbenner, 2014).

Body mass index (BMI). For the clinical samples, BMI was calculated from the height and weight data recorded on the day of admission by medical staff. For the control sample, participants' height and weight was measured on arrival at the laboratory, and the participant then entered these into the online questionnaire.

Perfectionism**.** To assess perfectionism, we used the concern over mistakes (CM) and personal standards (PS) subscales from the Frost Multidimensional Perfection Scale (FMPS: Frost, Marten, Lahart, & Rosenblate, 1990). The CM subscale consists of 9 items (sample item 'I hate being less than the best at things') and the PS subscale contains 7 items (sample item 'I have extremely high goals'). Items are rated on a 5-point Likert scale (1 = disagree strongly, 5

= agree strongly). Higher scores indicate higher endorsement of perfectionistic tendencies. Internal consistency of the FMPS has been demonstrated. In a recent study of individuals with BN, Cronbach's alphas for the CM and PS subscales were .89 and .83 respectively (Steele et al., 2011).

***Set-shifting*.** Set-shifting was assessed with the TMT (Reitan, 1955), one of the most frequently used neuropsychological tests in research and clinical practice (Rabin, Barr, & Burton, 2005) and more specifically in the eating disorder field (Roberts et al., 2007). For the current study, the electronic version of the TMT that was used is based on software code which is freely available from the Psychology Experiment Building Language database (Mueller & Piper, 2014). The TMT requires participants to first connect a 25-item numerical sequence in order (Trail A; 1-2-3 etc) then a 25-item alphanumeric sequence (Trail B; 1-A-2-B-3-C etc). The PEBL program allows researchers to choose either a random trail sequence, in which the sequence in Trail B changes each time the program is used, or one can choose to use the sequence that appear in the original pen-and-paper trails (Reitan, 1955). We used the latter approach for this study.

Four different measures were derived from the TMT. First, the total time taken to complete Part A of the TMT (Part A) which is generally considered to measure visual search and motor speed (Crowe, 1998). Second, the time taken to complete Part B of the TMT (Part B) which is considered to measure higher level cognitive functions, including set-shifting (Bowie & Harvey, 2006). Third, a frequently used measure of set-shifting is the total time taken to complete Part B minus that to complete Part A (Part B-A) which controls for baseline motor speed. Finally, the electronic version of the TMT records the exact number of clicks a participant makes while attempting the trail which generates an accuracy score (i.e., the number of targets, in this case 25, divided by the total number of clicks). The accuracy when

completing part B (Accuracy B) is of particular interest, as it gives information about perseveration, which refers to a repetitive response to a previously learned rule that persists even when a change occurs requiring a different response (Tchanturia et al., 2012).

3.3.3 Statistical analysis.

All analyses were conducted using SPSS v22.0. The two samples were first examined to determine whether scores on variables of interest were roughly normally distributed. No excessive violations were detected.

First, to compare the three groups (AN, BN and controls) on the baseline variables of interest, one-way between groups ANOVAs were run. Post-hoc testing was carried out using Hochberg's GT2 and Gabriel tests, as these are considered to be the most appropriate post-hoc tests for use when sample sizes are not equal (Allen & Bennett, 2012).

To compare the AN subtypes (AN-R vs AN-BP) on measures of set-shifting, linear regressions were run with the relevant set-shifting variable as the dependent variable. AN subtype was then entered in the second block. When comparing the two AN subtypes, BMI was not entered in the first block, as an independent samples *t*-test showed that BMI did not differ between these groups.

Next, to compare the performance of the clinical groups with the control sample, one-way between groups ANCOVAs were run. Age, BMI and EDE-Q global score were included as covariates. Effect sizes were calculated for all results. For between-groups analyses, Cohen's *d* was used. To ensure that the differences in sample sizes between the control and clinical groups would not influence these calculations, we employed a method that weighted effect sizes by the sample size of each group.

In order to explore the moderating effect of the selected predictor variables (perfectionism and eating disorder severity) on set-shifting performance, hierarchical

regression analyses were run. To prepare the data for these analyses, all continuous predictor variables were centred around their mean. Next, to manage the categorical group predictor variable (i.e., AN versus BN versus controls), two dummy variables were created. Group by predictor interaction terms were then calculated by multiplying each dummy variable by the predictor variable. On the first step of the regression, age and BMI were entered as potential covariates. On the next step, covariates and all individual predictor variables were entered. On the final step, the group by predictor interaction terms were also introduced. The TMT variable in question was the dependent variable. For the predictor analyses, the *Beta* correlation coefficient was calculated as a measure of effect size.

3.4 Results

3.4.1 Descriptive statistics.

A full description of each sample is given in **Table 3.1.** The clinical samples differed significantly from the healthy controls on measures of age (clinical > control), BMI (clinical < control) and on all EDE-Q scales, with the clinical samples showing elevated scores on all measures.

3.4.2 Eating disorder subtype differences on set-shifting variables.

The AN-R and AN-BP groups did not differ significantly on any TMT measure, as shown in **Table 3.2.**

3.4.3 Clinical versus control group differences on set-shifting variables.

As shown in **Table 3.3**, the BN group performed significantly worse on all measures (with the exception of Part A) compared to both the control and AN groups. The effect sizes for these differences were medium to large (*Cohen's d* = 0.66 and 0.90). The AN sample did not differ significantly from controls on any measure.

3.4.4 Predictors of set-shifting performance.

As shown in **Table 3.4,** personal standards perfectionism was a univariate predictor of performance on both Part A and Part B measures across groups, and was approaching significance for the Part B-A measure (p = .080). A higher personal standards score was associated with better performance on all set-shifting measures. Effect sizes were small.

There was only one significant group by predictor interaction, namely concern over mistakes by group predicted the Accuracy B score. As shown in **Figure 3.1,** post-hoc testing revealed that for the BN group only, lower concern over mistakes was associated with lower accuracy, whereas higher concern over mistakes was associated with higher accuracy. Simple slopes analysis revealed that this effect was significant (t = -3.37, p = .001). For the AN and control groups, there were no significant differences in Accuracy B as a function of concern over mistakes score.

3.5 Discussion

The purpose of the current study was to examine whether eating disorder subtype (AN vs BN and AN-R vs AN-BP) and perfectionism would predict set-shifting performance, as measured by the TMT, in a clinical sample. Contrary to our hypothesis, the AN-BP group did not differ from the AN-R group in performance on TMT measures. Our results are consistent with other studies that failed to detect differences between AN subtypes (Abbate-Daga et al., 2014; Tchanturia et al., 2004; Van Autreve et al., 2013), but contradict the conclusions of a recent meta-analysis that found evidence of sub-optimal set-shifting performance in AN-R but not in those with AN-BP (Wu et al., 2014). Given the ongoing lack of clarity around this issue, further investigation into set-shifting differences between the AN subtypes is warranted.

Also contrary to our hypothesis, the BN sample performed significantly worse than the AN sample and the control sample on all measures, with medium to large effect sizes. This is consistent with a previous comparison of individuals with an eating disorder with respect to

measures of set-shifting (Roberts et al., 2010), which found that the BN group performed more slowly than both AN subtypes and controls. While there was no significant difference noted for the computerised TMT measures of set-shifting performance there was a trend for the BN group and the unaffected sisters of the BN group to do worse than the healthy control. This study also suggested that the AN group was indistinguishable from controls on the TMT measures, as did the current study. This finding contradicts numerous earlier studies that have reported problems with set-shifting in individuals with AN, including many that have employed the same TMT measures as the current study (Stedal, Frampton, Landrø, & Lask, 2012). One possible explanation for this is that many studies report only performance on Part B of the TMT as a measure of set-shifting, rather than Part B-A. This is problematic, as using Part B alone does not control for baseline motor speed. It is possible therefore that some of the previously reported inefficiencies in AN may be influenced by poorer motor speed rather than pure set-shifting. It will be important to ensure that future research carefully controls for factors such as baseline motor speed.

The current finding regarding the inefficiencies on the TMT in the BN group is also interesting in light of evidence around the contribution of age to set-shifting performance. Adolescents with AN have been shown to perform better than adults on set-shifting measures compared to adults, and a number of studies have found that adolescents were indistinguishable from healthy controls (Lang et al., 2014). However, the older profile of our AN group compared to our BN group did not appear to influence our result. Indeed, our BN group had a much higher proportion (34.8%) of adolescent patients (those 19 years or under), compared to the AN group (17.9%), but nonetheless exhibited poorer set-shifting performance. This suggests that age may not be a protective factor in the case of set-shifting in BN, and does not support the finding that chronicity may impact on set-shifting (Roberts et al.,

2010). Taken together, these findings highlight the need for ongoing investigation into the nature and magnitude of set-shifting inefficiencies in BN, as our findings suggest that poor set-shifting is associated with the disorder and not behaviours or chronicity.

Overall, our hypothesis that elevated perfectionism would be associated with poorer performance on TMT measures was not supported. Rather, higher personal standards perfectionism predicted superior performance for all measures other than accuracy, across the three experimental groups. Although Lindner et al. (2014) also reported that higher personal standards was associated with better set-shifting, this was only the case for their control group, while in the recovered AN group, higher personal standards was associated with slower times. Also contrary to our hypothesis, concern over mistakes perfectionism was only associated with performance on one measure of set-shifting, namely accuracy. This effect was only noted in individuals with BN, who showed greater accuracy as their concern over mistakes score increased. Some discussion of the failure of our results to show any link between elevated perfectionism and poor set-shifting is warranted. It is possible that perfectionism alone might be insufficient for understanding the nature of disordered eating, and it has been suggested that two related concepts, namely persistence and perseveration, might be important adjuncts (Serpell, Waller, Fearon, & Meyer, 2009). In particular, persistence (pursuing goal directed behaviour even when this is difficult or laborious) was found to be significantly lower in AN and BN groups compared with controls in a recent study, while no differences in perfectionism (measured using the Persistence, Perseveration and Perfectionism Questionnaire: Serpell et al., 2009) between groups were noted (Waller et al., 2012). Although our clinical groups did score more highly on perfectionism measures compared to controls, the addition of these other two measures may have been necessary to predict set-shifting performance. Our result also speaks to the issue of measurement instruments: since

perfectionism can be conceptualised and measured in different ways (Hewitt, Flett, & Ediger, 1995), it would be valuable to further investigate the relationship between perfectionism and set-shifting with a wider range of measures to clarify how the various dimensions of perfectionism may be implicated.

The results of the current study should be interpreted in light of several limitations. First, our control group was larger than our clinical group. Although we employed statistical measures that correct for this, the power associated with our clinical samples was more limited than that of our control group. This was particularly the case in the comparison of the AN subtypes, as the AN-BP group had only 9 cases. Repeating these analyses with larger samples would provide more rigour to these findings. Second, although the educational status of our control group was known to us, we did not have data on the educational status in the clinical group, which might have affected performance on the TMT (Lezak, 2004). Although the results of several studies have suggested that such effects are only applicable to people with severe limitations in educational attainment, (Drane, Yuspeh, Huthwaite, & Klingler, 2002; Hamdan & Hamdan, 2009), controlling for educational status in clinical groups would be an important addition in future research. Third, we only employed one measure of set-shifting, namely the TMT. While the TMT has been shown to correlate well with related measures of executive functioning (Chaytor, Schmitter-Edgecombe, & Burr, 2006; Strauss, Sherman, & Spreen, 2006), no single test can be considered as a complete measure of cognitive flexibility, and these results can only be considered in relation to use of the TMT. Replication of these results across a range of different measures would allow for stronger conclusions about the differences between the groups. Fourth, given the non-medical focus of the hospital program, the BMI of the AN group in our clinical sample was rather moderate ($M = 16.51$, $SD = 1.60$), which may have lessened any potential effects of acute starvation present in those with very

low BMIs. However, low BMI in women with AN was not associated with set-shifting in one study (Tchanturia et al., 2011), and weight recovery did not lead to improved set-shifting performance for individuals with AN (Tchanturia et al., 2004; Tenconi et al., 2010). We did not have data on diagnostic crossover between AN and BN in the clinical sample, and were therefore not able to separate the BN group into those with a previous diagnosis of AN and those without. Examination of this question in a larger sample would be important to determine if the two profiles differ. Fifth, given our relatively small numbers of clinical participants, our analyses do not control for the possible presence of confounding variables such as comorbid major depression or anxiety which may also impact performance. Related to this point, no data on illness chronicity were available. Finally, given our clinical sample only included hospitalised patients, it is not possible to generalise our results to outpatient cases.

In conclusion, set-shifting performance in our sample was more impaired in individuals with BN, but less pronounced in AN, than previously shown. If replicated, these results may have important implications for our understanding of the cognitive profiles of patients with eating disorders, and for the development of brain-directed prognostic tools and interventions. Future research should continue to investigate differences in set-shifting across eating disorder subtypes using larger samples and a wider range of measures.

Table 3.1

Descriptive statistics by group.

	AN n = 28	BN n = 23	Control n = 149	ANOVA
	M (SD)	*M (SD)*	*M (SD)*	*F (p)*
Age	25.96 (7.85)[a]	23.04 (5.92)[b]	19.25 (1.66)[c]	42.09 (<.001)
BMI	16.15 (1.60)[a]	22.94 (3.48)[b]	22.62 (4.11)[b]	35.45 (<.001)
EDE-Q global	4.83 (0.89)[a]	4.73 (0.95)[a]	1.84 (1.12)[b]	142.66 (<.001)
Perfectionism (CM)	3.94 (0.83)[a]	4.13 (0.48)[a]	2.59 (0.89)[b]	55.42 (<.001)
Perfectionism (PS)	3.76 (0.88)[a]	3.85 (0.64)[a]	3.24 (0.83)[b]	8.81 (<.001)

Note: Superscripts are used to indicate significant differences between groups. EDE-Q = Eating Disorder Examination – Questionnaire, CM = concern over mistakes, PS = personal standards

Table 3.2

Results of linear regressions with AN subtype (AN-R vs AN-BP) as the independent variable and TMT variables as the dependent variables, controlling for BMI.

	t (p)	*Cohen's d*	*AN-R (n = 19) M(SD)*	*AN-BP (n = 9) M(SD)*
Part B-A	0.04 (.968)	0.08	25.25 (10.26)	24.42 (9.65)
Part A	-0.83 (.417)	0.33	29.26 (7.89)	26.78 (6.31)
Part B	-0.47 (.644)	0.19	54.51 (13.10)	52.19 (10.04)
Accuracy B	-1.57 (.129)	0.63	97.50% (5.67%)	92.72% (10.62%)

Table 3.3

ANCOVA[1] results between the three groups, post-hoc tests and descriptive statistics by group for each TMT variable and between group effect sizes (d) where p<.05.

Variable	AN	BN	HC	ANCOVA		
	M (SD)	*M (SD)*	*M (SD)*	*F*	*p*	Post-Hoc comparisons
Part B-A	25.30 (9.89)	38.07 (23.25)	27.77 (14.90)	4.73	**.010**	BN>HC (*d* = .64) BN>AN (*d* = .74)
Part A	28.46 (7.39)	28.63 (7.38)	4.68 (6.60)	1.19	.307	---
Part B	53.77 (12.06)	66.70 (25.82)	51.13 (15.67)	5.55	**.005**	BN>HC (*d* = .90) BN>AN (*d* = .66)
Accuracy B	95.96 % (7.74 %)	84.93 % (17.86 %)	94.09 % (9.01 %)	9.63	**<.001**	BN<HC (*d* = .87) BN<AN (*d* = .83)

[1]ANCOVA controlling for BMI, age and EDE-Q global score

Table 3.4

Results of final step of moderated regression analyses for all samples combined examining potential predictors of set-shifting variables.

	Part B-A		Part A		Part B		Accuracy B	
	t (p)	*Beta*	*t (p)*	*Beta*	*t (p)*	*Beta*	*t (p)*	*Beta*
ED pathology (EDE-Q)								
Age	-0.53 (.598)	-.044	1.94 (.054)	.158	0.29 (.771)	.024	1.47 (.143)	.120
BMI	-0.17 (.868)	-.015	-0.27 (.798)	-.022	-0.26 (.799)	-.023	1.24 (.216)	.109
EDE-Q global	-0.34 (.732)	-.046	0.83 (.410)	.107	0.02 (.987)	.002	-0.20 (.843)	-.026
Dummy group variable 1	-1.12 (.265)	-.222	0.88 (.382)	.168	-0.67 (.502)	-.132	0.25 (.802)	.049
Dummy group variable 2	**2.03 (.043)**	.349	0.98 (.330)	.163	**2.25 (.026)**	.381	**-3.39 (.001)**	-.567
Dummy group 1 x EDE-Q	1.20 (.232)	.230	-0.47 (.641)	-.087	0.91 (.364)	.172	0.13 (.898)	.024
Dummy group 2 x EDE-Q	-0.64 (.522)	-.114	-0.18 (.859)	-.031	-0.66 (.512)	-.116	*1.73 (.086)*	.299
Perfectionism (CM)								
Age	-0.23 (.820)	-.020	**2.05 (.041)**	.171	0.62 (.538)	.052	0.77 (.441)	.064
BMI	-0.18 (.859)	-.014	0.21 (.835)	.016	-0.08 (.937)	-.006	1.09 (.279)	.086
CM	-0.89 (.376)	-.085	-1.17 (.245)	-.108	-1.28 (.201)	-.120	1.17 (.244)	.108
Dummy group variable 1	-1.11 (.269)	-.132	**2.10 (.037)**	.242	-0.17 (.862)	-.020	0.48 (.635)	.055
Dummy group variable 2	**2.93 (.004)**	.526	*1.66 (.098)*	.290	**3.36 (.001)**	.593	**-3.94 (<.001)**	-.686
Dummy group 1 x CM	1.40 (.164)	.158	-0.31 (.759)	-.034	1.16 (.249)	.129	-0.39 (.700)	-.043
Dummy group 2 x CM	-1.59 (.114)	-.296	-0.30 (.766)	-.054	-1.58 (.117)	-.289	**2.05 (.042)**	.370
Perfectionism (PS)								
Age	-0.60 (.549)	-.050	*1.92 (.057)*	.155	0.22 (.829)	.018	1.46 (.147)	.119
BMI	-0.57 (.572)	-.046	-0.20 (.840)	-.016	-0.60 (.547)	-.048	1.41 (.160)	.113
PS	*-1.76 (.080)*	-.147	**-2.00 (.047)**	-.161	**-2.43 (.016)**	-.198	1.05 (.294)	.086
Dummy group variable 1	-0.62 (.534)	-.060	*1.83 (.069)*	.170	0.16 (.872)	.015	0.61 (.540)	.058
Dummy group variable 2	**2.02 (.045)**	.176	**2.54 (.012)**	.214	**2.88 (.004)**	.246	**-2.86 (.005)**	-.244
Dummy group 1 x PS	1.28 (.202)	.105	0.81 (.422)	.064	1.50 (.134)	.121	-0.62 (.535)	-.050
Dummy group 2 x PS	1.57 (.117)	.140	0.36 (.720)	.031	1.60 (.112)	.139	*-1.72 (.087)*	-.150

Note: dummy group variable 1 = AN versus BN/controls; dummy group variable 2 = BN versus AN/controls; bolded entries are significant; italicised have p<0.10, EDE-Q = Eating Disorder Examination – Questionnaire, CM = concern over mistakes, PS = personal standards

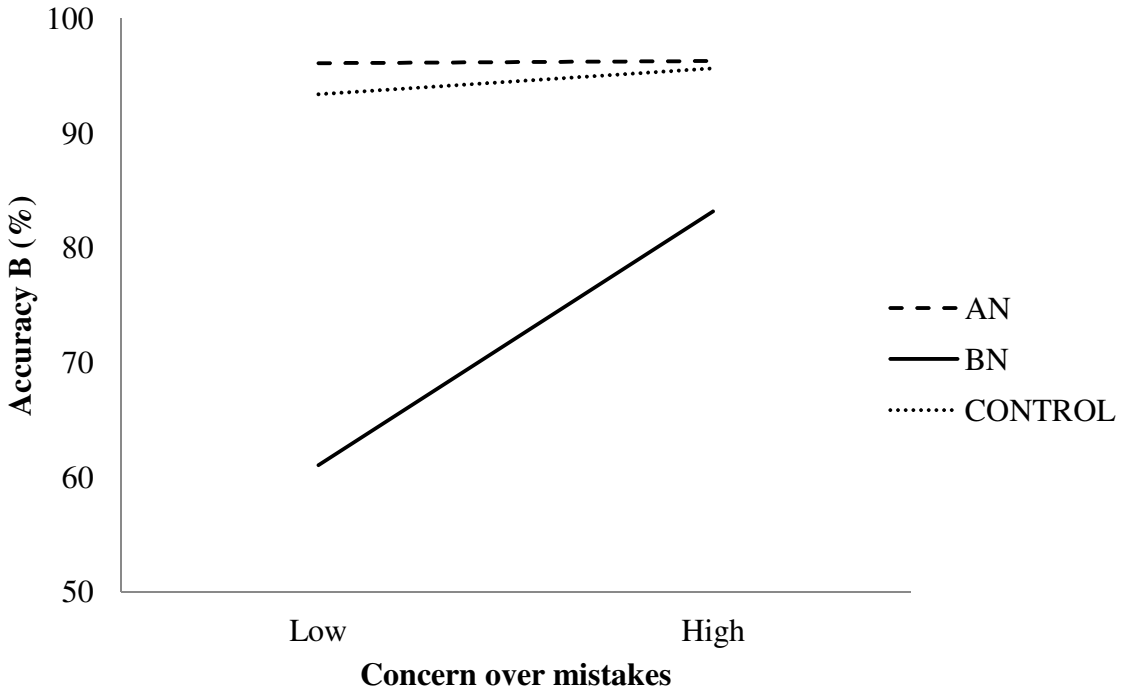

Figure 3.1 Accuracy B scores for all groups by level of concern over mistakes.

Chapter 4

Predictors of treatment outcome in adolescent inpatients with anorexia nervosa[3]

[3] Material from this chapter has published in *Clinical Psychologist* [Vall, E., & Wade, T. D. (2016). Predictors and moderators of outcomes and readmission for adolescent inpatients with anorexia nervosa: A pilot study. *Clinical Psychologist*.]

4.1 Abstract

Objective: This pilot study investigated predictors, moderators and mediators of outcome and readmission in adolescents receiving specialist inpatient treatment for anorexia nervosa.

Method: Adolescents (n = 40) aged between 14 and 17 years (mean = 15.42) were assessed at admission and discharge from a specialist inpatient program, and again at 3-month follow-up on the following outcome variables: eating disorder pathology, quality of life, and BMI centile. Readmissions to hospital were recorded over the 3-months post-discharge period. Potential predictors were drawn from theoretical models.

Results: Readmission during the three-month follow-up period was less likely for first presentations. Higher baseline purging, concern over mistakes perfectionism, ineffectiveness and mood intolerance were associated with higher levels of eating disorder pathology and poorer quality of life over all points of follow-up. Driven exercise moderated weight outcomes such that higher levels of baseline exercise resulted in a lower BMI centile at follow-up. Greater weight gain during treatment predicted higher BMI centile at follow-up, and increased perfectionism during treatment predicted a greater likelihood of being readmitted within 3 months of discharge.

Conclusions: Robust weight gain during inpatient treatment should be encouraged to improve later weight outcomes. Focusing on the prevention of growth in perfectionism may be useful in improving psychological outcomes, as will prioritising the elimination of purging and improved emotional regulation and self-efficacy. Efforts should be made to reduce driven exercise to promote better weight-related outcomes.

4.2 Introduction.

The adverse impacts of anorexia nervosa (AN) are particularly dangerous for adolescents given the heightened potential for long term damage during this critical developmental period (Golden et al., 2003). As well as a 12-fold increase in mortality rate for females aged 15-24 years with AN (Arcelus, Mitchell, Wales, & Nielsen, 2011), medical complications include growth retardation, osteoporosis, infertility and cognitive impairment (Katzman, 2005). Functioning is affected across social, vocational and educational domains (Hay & Mond, 2005; Mond et al., 2004). The economic impact associated with AN is also profound, due in large part to the frequent necessity of life-saving inpatient treatment, particularly for young sufferers (Striegel-Moore et al., 2008; Thompson et al., 2004). In Australia this burden falls primarily on public health systems, with around 90% of inpatient admissions for AN being to public hospitals (AIHW, 2011). Promptly and effectively treating AN in adolescents is essential to mitigate these impacts, however outcomes in existing treatments remain sub-optimal. Two years after inpatient or outpatient treatment, 27 percent of adolescents continued to meet full criteria for AN and only 33 percent were fully recovered (Gowers et al., 2007). Ten years following inpatient treatment, only 69 percent of adolescents were recovered (Herpertz-Dahlmann et al., 2001).

One potential approach to improving these outcomes is to identify factors that predict treatment response. This strategy offers two benefits: first, it may help to identify individuals who are at risk of poor outcome, and second, it can identify treatment components or processes that could be modified to improve efficacy across the population. Despite the potential of this approach, it has not been widely pursued in eating disorder research, particularly in the adolescent arena. One review of treatment outcomes for adults with AN failed to find any convincing predictors of outcome (Bulik et al., 2007), while another reported that the presence of mood/anxiety disorders and impaired social functioning were at best ‘moderately’

successful in predicting outcome for adults with either AN or bulimia nervosa (BN) (Berkman et al., 2007). Across AN, BN and other specified feeding and eating disorders (OSFED) diagnoses, greater symptom severity was linked to a poorer outcomes at 12 month follow-up (Richard et al., 2005). Finally, the most recent review and meta-analysis of outcomes across all eating disorder diagnoses and age groups (Vall & Wade, 2015a) found that while several baseline predictors were associated with better outcomes, there was generally large inter-study variability in effect sizes, and outcomes were operationalised in different ways across studies, making it difficult to effectively compare results.

Another limitation of the literature is that there has been relatively little examination of complex predictor pathways, in particular moderators and mediators of outcome. A moderator is a baseline characteristic that can be shown to have an interactive effect with treatment on the outcome, while mediators are changes in variables that occur after the commencement of treatment to predict outcome (Kraemer, Kiernan, Essex, & Kupfer, 2008; Kraemer et al., 2002). These complex predictor types are important, as they allow us to more precisely identify individuals at risk of a poor outcome and intervene accordingly, and provide greater insights into how treatments might best be modified for particular subgroups, or which facets of psychopathology might best be targeted during treatment to achieve better outcomes. In one of the few studies to examine moderators of treatment outcome, having higher eating related obsessionality or coming from a single-parent household, coupled with a longer (versus a shorter) form of outpatient family based therapy (FBT), predicted better outcomes relating to weight and eating pathology (Lock et al., 2005). In a more recent study, having higher baseline levels of eating related obsessionality or eating disorder pathology and receiving FBT (versus adolescent focused therapy), was associated with a greater likelihood of remission at end of treatment, but not at follow-up (Le Grange et al., 2012). In the same study, individuals with the

binge/purge subtype who received FBT were more likely to achieve remission at follow-up. Outside of controlled trials that seek to compare outcomes across different treatment modalities, an understudied moderational process within a treatment is the interaction between levels of a baseline variable and time. This kind of analysis can detect group differences that may emerge at different points in treatment. A benefit of such insight is that it can assist clinicians to identify critical periods when deterioration might be likely to occur for certain individuals, or when interventions might be particularly timely.

An area that has received some attention in the adolescent literature is symptom change during outpatient treatment as a predictor of outcome. For example, weight gain in the early stages of treatment has been shown to predict better outcomes including weight and eating pathology at end of treatment (Doyle et al., 2010; Le Grange, Accurso, Lock, Agras, & Bryson, 2014) and 12 month follow-up (Lock et al., 2006). Change in depression and self-esteem have also been examined as potential predictors in one study, but change by the fourth week of treatment did not predict remission (Le Grange et al., 2012). To our knowledge, change in symptoms during treatment as a predictor of outcome for adolescents receiving inpatient treatment for AN, has not been examined.

Given the gaps in our ability to predict treatment outcomes for adolescents with AN, the aim of this pilot study was to examine a range of predictors (including symptom change during treatment) and moderators of symptom change over time in an inpatient sample. To ensure a theoretically-informed approach to this question, putative predictors were chosen based on two prominent theoretical models of AN, namely the Transdiagnostic Model (Fairburn et al., 2003) and the Cognitive Interpersonal Model of AN (Schmidt & Treasure, 2006). Given the large number of potential maintaining factors indicated across the two models, it was not feasible to test the models fully, so we examined those variables that are shared between both models.

Specifically, the models share the position that perfectionism and cognitive rigidity, ineffectiveness and mood intolerance contribute to the maintenance of eating disorder symptomatology.

We hypothesised that individuals with more severe baseline symptoms would have poorer outcomes at follow-up compared to those with less severe presentations. It was predicted further that higher levels of baseline symptoms would moderate outcome over time, such that poorer outcomes would be recorded at all time points. Finally, it was predicted that greater improvements in weight and related psychopathology during treatment would predict better outcomes.

4.3 Method

4.3.1 Participants and treatment setting.

The research took place in the Paediatric Inpatient Unit at Flinders Medical Centre, a large public and teaching hospital located in the southern metropolitan area of Adelaide. A specialist inpatient eating disorder program was introduced in 2013 and has been described in detail elsewhere (Suetani, Yiu, & Batterham, 2015). Briefly, the inpatient program includes the input of paediatrics, psychiatry, Child and Adolescent Mental Health Service (CAMHS) workers, nursing, dietetics, physiotherapy, occupational therapy, diversional therapy and teaching. Patients are admitted either via the hospital's emergency department or the paediatric outpatient clinic. The structure of the program entails a stepped approach beginning with management of medical instability. The medical stabilisation admission criteria are described in detail by Suetani et al (2015). The program then graduates through the withdrawal of enteral feeds to a full oral feeding, establishing normal eating with families by gate passes as part of transition from home to hospital. Progression through each stage is dependent on the patient making appropriate progress. Patients are weighed twice a week, and on these days the team meets to discuss patients' progress and clinical management. Patients and their families attend

a family meeting with the treating team once a week. Discharge criteria are established for each patient following admission and generally include attaining medical stability, meeting a safe minimum weight and showing evidence of behavioural change.

Study inclusion criteria required patients to be 14 years or over, to have a diagnosed eating disorder, and deemed to be medically fit for participation by the medical treatment team. Forty-five unique patients were admitted to the eating disorder program during the research period. Of these, three were excluded as they were under 14 years, and two were excluded because their parents did not consent to their involvement in the study, leaving 40 cases (89% of those admitted) available for analysis. Participants were only included in the dataset once, so were not assessed again if they were readmitted during the study period.

4.3.2 Procedure.

The project was approved by the Southern Adelaide Clinical Human Research Ethics Committee. Written informed consent was obtained from all patients and parents. The self-report measures were administered at admission and discharge by a researcher on the ward. Admission and discharge weight were recorded from hospital charts. For the follow-up assessment, the questionnaire was emailed to participants 3-months post-discharge. For patients who did not complete the follow-up assessment, follow-up weight was obtained from hospital charts where possible.

4.3.3 Measures.

Body mass index (BMI) centile. BMI centile was calculated by entering height, weight, date of birth and date of weighing into a standardised tool obtained from the Centre for Disease Control and Prevention (2010).

Eating pathology and behavioural features. The Eating Disorder Examination Questionnaire (EDE-Q: Fairburn and Beglin, 1994) was administered to confirm eating

disorder diagnosis (APA, 2013) and to assess eating disorder symptom severity, including frequency of purging (i.e., laxatives, vomiting, diuretics) and driven exercise. The EDE-Q is a 28-item self-report questionnaire with that assesses both cognitive and behavioural indicators of eating disorders, where a higher global score indicates more severe eating pathology. Internal consistency of the global score in the current sample was demonstrated by a Cronbach's alpha of .95.

Quality of life. Eating disorder related quality of life (QOL) was measured using the Clinical Impairment Assessment (CIA: Bohn et al., 2008), a 16-item self-report measure of the severity of psychosocial impairment due to eating disorder features. Higher scores indicate higher impairment. Internal consistency of the measure in the current sample was demonstrated by a Cronbach's alpha of .93.

Perfectionism. Two measures of perfectionism were used, namely the concern over mistakes (CM) and personal standards (PS) subscales from the Frost Multidimensional Perfection Scale (Frost, Marten, Lahart, & Rosenblate, 1990). Higher scores indicate greater levels of perfectionism. Internal consistency of the measure in the current sample was demonstrated by Cronbach's alphas of .96 and .90 respectively.

Motivation. Motivation was measured using three questions: 'How motivated are you to recover?', 'How ready are you to change your eating and weight?', and 'If you decided to change, how confident are you that you would succeed?'. Responses were made on a 100-point visual analogue scale.

Self-efficacy. Self-efficacy was measured with the 10-item self-report ineffectiveness subscale of the Eating Disorder Inventory-2 (EDI-I) (Garner, 1991) with higher scores indicating greater feelings of inadequacy, insecurity, worthlessness and having no control over

one's life. Internal consistency of the measure in the current sample was demonstrated by a Cronbach's alpha of .90.

***Mood intolerance*.** Mood intolerance was measured with the Difficulties in Emotional Regulation Scale (Gratz & Roemer, 2004). The DERS is a self-report scale containing 36 items. Higher scores indicate more difficulties with emotion regulation, or greater intolerance of mood states. Internal consistency of the measure in the current sample was demonstrated by a Cronbach's alpha of .96.

***Cognitive-rigidity*.** Set-shifting was used as a measure of cognitive-rigidity, and was assessed with an electronic version of the trail making test (Reitan, 1955) freely available from the Psychology Experiment Building Language database (Mueller & Piper, 2014). Participants connect a 25-item numerical sequence in order (Trail A; 1-2-3 etc) then a 25-item alphanumeric sequence (Trail B; 1-A-2-B-3-C etc). The measure of set-shifting used in this study was the total time taken to complete Part B minus that to complete Part A, to control for baseline motor speed. This measure has been validated for use in adult inpatients with AN (Vall & Wade, 2015b).

4.3.4 Treatment outcome.

The main patient outcomes were change in BMI centile, eating disorder pathology and quality of life. Outcomes were measured at discharge and again at 3-month follow-up. The other outcome was readmission during the 3 months post-discharge. Readmission was defined as any admission of at least one night due to AN, at any of the public hospitals in South Australia.

4.3.5 Analytic Strategy.

To investigate predictors of readmission, binary logistic regressions were conducted, with readmission coded as either Yes (at least one readmission) or No (no readmissions). To

investigate predictors and moderators of weight gain, eating pathology and quality of life over time, linear mixed modelling was used. This approach was selected as it preserves the number of cases included in analyses rather than excluding cases with missing data (Nich & Carroll, 1997). It employs maximum likelihood (ML) estimation which is considered a more accurate method of dealing with missing data than other methods such as the *expectation–maximization (EM)* algorithm. The analysis was first run for the sample as a whole, then again just including those patients who did not require readmission during the 3-month follow-up period.

In order to understand whether any variables moderated response over time, two-way interactions involving time were examined first where the main effect of time and the predictor was entered, followed by an interaction between time and the predictor. To adjust for multiple testing and control for the family wise error rate, the Bonferroni adjustment procedure was employed, where results were only considered significant where the *p* value was less than .05/number of variables tested.

To determine whether change in baseline variables predicted outcome, we used linear regression. First, change variables were created for each predictor variable between admission and discharge. These change scores were used as the predictor variables. To capture change in outcome variables over time, change variables were also computed for each dependent variable, such that outcome was the overall change in each dependent variable between admission and follow-up.

To understand the difference in outcomes for individuals with high or low scores on a predictor variable, post-hoc testing was conducted whereby the sample was divided using median split. The correlation coefficient, r, was calculated as a measure of effect size for key outcomes, where r = .10 constitutes a small effect, r = .30 a medium effect, and r = .50 a large effect (Cohen, 1992). Correlation coefficients were chosen as the effect size metric because

they have been shown to best enable interpretation of the practical importance of an effect (Field, 2001).

4.4 Results

4.4.1 Patient characteristics.

Twenty-six patients (65%) were first-time presentations to the unit. Eight patients had between 1-2 prior admissions, three had 3-5 prior admissions, and a further three had had more than 5 previous hospitalisations. The average illness duration was 1.23 years (SD = 1.39). The average age was 15.40 years (SD = 1.01, minimum 14 years, maximum 17 years). Thirty-six (90%) of the participants had the AN-restrictive subtype, the remaining four were diagnosed as AN-binge/purge subtype. The sample was predominantly female (n = 38, 95%) and Caucasian (n = 37, 92.5%). The average length of stay was 20.10 days (SD = 10.34).

4.4.2 Key outcome variables.

The follow-up completion rate was 70 % (n = 28). Follow-up weight was available from hospital charts in a further 20 % (n = 8) of cases. In the three months post-discharge, 30% of the sample (n = 12) were readmitted at least once. For the entire sample, there was a significant increase in mean BMI centile between admission and the three-month follow-up, but not in eating disorder pathology or quality of life, as shown in **Table 4.1**. Also shown in **Table 4.1,** for those who did not require readmission during the follow-up period, quality of life increased significantly in addition to BMI centile.

4.4.3 Predictors of readmission.

As shown in **Table 4.2**, there was only one predictor of readmission in the 3 months post-discharge. Specifically, individuals who were first-time presentations were less likely to be readmitted during the follow-up period compared to those with multiple previous admissions.

4.4.4 Baseline predictors and moderators over time of outcome.

BMI centile. As shown in **Table 4.3,** there were no baseline predictors of BMI centile. However, baseline exercise frequency moderated BMI centile over time (**Figure 4.1**), where individuals who reported more exercise at baseline had a lower BMI centile, but this difference only emerged at follow-up. The high and low exercise groups did not differ on BMI centile at admission or discharge.

Eating disorder pathology. There were no moderators with time of eating disorder pathology, but a number of variables emerged as significant baseline predictors, outlined in **Table 4.3.** Higher baseline purging, concern over mistakes perfectionism, ineffectiveness and mood intolerance were associated with more severe symptoms at all time points. Conversely, having higher motivation and readiness to recover was associated with less severe symptoms at all time points. Differences in eating disorder pathology for individuals scoring high and low on each of these variables at each time point are given in **Table 4.4.** Three variables lost significance after adjusting for multiple testing, namely confidence to recover, driven exercise and set-shifting.

Eating related quality of life. After adjustment for multiple testing, there were no moderators with time of quality of life. In terms of baseline predictors, higher baseline purging, eating disorder pathology, concern over mistakes perfectionism, ineffectiveness and mood intolerance, were associated with poorer quality of life at all time points. Conversely, having higher motivation to recover was associated with better quality of life at all time points. Differences in quality of life scores for individuals scoring high and low on each of these variables at each time point are given in **Table 4.4.** Three variables lost significance after adjusting for multiple testing, namely readiness to recover, personal standards perfectionism and set-shifting.

4.4.5 Symptom change as a predictor of outcome.

Change in two variables emerged as significant predictors of outcome. First, greater increase in BMI centile between admission and discharge was associated with a greater overall increase in BMI centile over time to follow-up *(t* = 2.61, *p* =.013, *r* = .39). Second, an increase in personal standards perfectionism between admission and discharge was associated with a greater likelihood of being readmitted in the 3 months following discharge (*t* = 2.31, *p* = .026, *r* = .35).

4.5 Discussion

This pilot study examined predictors of outcomes in adolescents who received specialist inpatient treatment for AN. Specifically we sought to identify theoretically-informed predictors and moderators of outcomes, and also examined whether change in symptoms during treatment predicted outcomes. Outcomes included change in weight, eating pathology and quality of life, as well as readmission during the follow-up period.

The role of perfectionism in predicting outcomes for this group was important across several outcome measures, with higher baseline concern over mistakes being associated with lower BMI and reduced quality of life at all time points. Moreover, an increase in personal standards between admission and discharge was associated with greater likelihood of readmission within 3 months. Taken together, our findings are consistent with previous literature that reported a negative association between perfectionism and outcome (Bizeul, Sadowsky, & Rigaud, 2001; Sutandar-Pinnock, Blake Woodside, Carter, Olmsted, & Kaplan, 2003). In terms of clinical utility, our results suggest that perfectionism may be harmful if left unchecked. Given a large body of evidence showing that perfectionism is modifiable (Lloyd, Fleming, Schmidt, & Tchanturia, 2014), one potentially useful approach would be to target perfectionism in an effort to neutralise its harmful side effects in the maintenance of ongoing psychopathology, while redirecting the desire to achieve high standards away from AN and

toward achievable standards in other life domains that have been sidelined by illness. This is the approach suggested for the treatment of clinical perfectionism (Egan, Wade, Shafran, & Antony, 2014), which is postulated to be a risk factor for a variety of psychopathologies.

Our finding that weight gain between admission and discharge predicted a higher weight at follow-up builds on the existing literature which suggests that weight gain in outpatient treatment is important in predicting later weight outcomes (Doyle et al., 2010; Le Grange, Accurso, et al., 2014; Lock et al., 2006). As these studies all involved outpatient samples, our results indicate that the same trend may be true for inpatient populations. From a clinical perspective, the current result suggests that inpatient protocols should strive towards the greatest possible weight gain that is safely possible during admission. Further, those individuals who gain less weight during admission may need to be more actively followed-up to ensure that their progress monitored and that further intervention be provided if necessary.

The contribution of driven exercise frequency to outcome deserves further investigation. In the current study higher baseline levels predicted poorer weight outcomes over time, but few other studies have examined the impact of driven exercise on outcome in adolescents with AN. Driven exercise at baseline in adolescent outpatient treatment for AN did not predict weight at end of treatment (Stiles-Shields, Bamford, Lock, & Le Grange, 2015), but in that study no follow-up was reported, so it is unclear if changes between the groups emerged later as per our results. The same study did however find that driven exercise at baseline predicted worse eating pathology at end of treatment. In two separate inpatient studies of adults with AN, higher exercise at baseline predicted drop-out (El Ghoch et al., 2013) and less improvement in eating psychopathology by discharge (Dalle Grave, Calugi, & Marchesini, 2012). Taken together, these findings suggest that higher levels of driven exercise in patients with AN is likely to be detrimental to treatment outcome. Treatments approaches that include

outpatient interventions around exercise may be a useful addition for this population. Further, families should be encouraged to support their adolescent to refrain from driven exercise, and attempt to redirect exercise to more social and contained activities such as team sports.

Finally, although not predictive of change in outcome measures over time, a number of variables were associated with severity of psychopathology (but not BMI) at all time points. Having higher baseline purging, mood intolerance, eating pathology and lower quality of life, were generally associated with worse psychological state at all time points. By contrast, being more motivated, ready and confident to change, and having higher self-efficacy, was associated with a better psychological profile at all time points, consistent with findings from the adult literature (Vall & Wade, 2015a). This result raises two important considerations. From a research perspective, it underscores the importance of considering psychological wellbeing and quality of life in addition to weight in this population, as variations in these measures were apparent in the absence of weight differences. Second, it suggests that clinically targeting these variables at any time point may be helpful in improving psychological wellbeing in adolescents with AN.

4.5.1 Methodological considerations.

Several methodological limitations should be considered when interpreting these findings. First, although we had a number of significant results, the sample size was small, and it is therefore likely that some of the non-significant results reported here may attain significance with a larger sample size. As such, the present research should be considered as a pilot study, and future research should aim to replicate the analyses with larger participant numbers. Second, the follow-up period of approximately 3.5 months was relatively short. Repeating the follow-up measures at additional intervals would be helpful to identify predictors of outcome in the longer term. Third, we only had basic data about patients'

engagement with outpatient treatment during the follow-up period. We know that approximately 40% of patients receive follow-up services from a private psychiatrist or psychologist, 30% in hospital outpatient services, between 10-15% through local or regional CAMHS, with the remaining clients either pursuing miscellaneous services or not seeking further services. However, we did not have access to individualised data. This would be a valuable inclusion in future research to determine whether it might further moderate outcomes. Fourth, we did not have data on patient co-morbidity. Fifth, follow-up weight was primarily obtained via self-report. This may have impacted on the reliability of the measurement. Sixth, it should be noted that the models from which our predictors were drawn, and the measures employed to assess these constructs, were based on adult models of eating disorders. At present, there are no adolescent-specific models of eating disorders, however there is evidence that treatments that are based on the Transdiagnostic Model (Fairburn et al., 2003) are effective with adolescent populations (e.g., Dalle-Grave et al., 2013), and treatments based on the Cognitive Interpersonal Model (Schmidt & Treasure, 2006) have demonstrated efficacy with adolescents from 16 years of age (Wade, Treasure & Schmidt, 2011). Accordingly, in the absence of any adolescent-specific theory, we felt these adult models were justified. Finally, our sample included two male participants. While there is some evidence that adolescent males report lower weight and shape concern compared to females (Darcy, Doyle, et al., 2012), overall differences in terms of clinical characteristics appear to be minimal (Welch, Ghaderi, & Swenne, 2015). On balance, it was decided to include the male participants in the dataset, however future research with exclusively male samples would be extremely valuable.

4.5.2 Conclusions.

The present findings highlight several areas of potential clinical intervention. Both an inpatient and discharge focus on reducing purging, concern over mistakes and personal

standards perfectionism, and mood intolerance, will be important for improving psychological outcomes and therefore may prevent relapse. Where possible, reduction of driven exercise should be encouraged. Achieving robust weight gain during treatment is likely to improve weight outcomes in the longer term.

Table 4.1

Significant interactions in linear mixed models between time and change in dependent variables between baseline and follow-up for the whole sample and for those who had no readmissions.

	Admission		Discharge		Follow-up		Overall
	M (SE)	*r*	M (SE)	*r*	M (SE)	*F (p)*	*r*
Whole sample (N = 40)							
BMI centile	8.98 (2.07)[a]	.34	21.25 (3.13)[b]	.18	28.62 (3.34)[c]	**37.40 (<.001)**	.51
Eating pathology	3.94 (0.23)	.09	3.83 (0.26)	.11	3.53 (0.35)	1.28 (.299)	.21
Quality of life	2.06 (0.22)	.01	2.03 (0.25)	.26	1.70 (0.27)	2.85 (.080)	.25
Single admissions[1] (n = 28)							
BMI centile	8.16 (4.81)[a]	.31	18.88 (5.34)[b]	.20	26.93 (5.77)[c]	**24.86 (<.001)**	.48
Eating pathology	3.98 (0.25)[a]	.14	3.75 (0.20)[a]	.11	3.32 (0.29)[b]	2.21 (.145)	.22
Quality of life	2.09 (0.12)[a]	.09	1.90 (0.20)[a]	.27	1.62 (0.21)[b]	**3.90 (.042)**	.32

Note: Significant results are indicated in bold text. Different superscripts indicate significant post-hoc differences between time points.
[1]Single admissions were those with no readmissions during the 3-month follow-up period.

Table 4.2

Predictors of readmission (Yes vs No) during the 3 months post discharge.

	Wald (p)	*Exp (B)*	*r*
Demographic variables			
Age	0.10 (.756)	1.12	.05
Duration	3.16 (.075)	1.89	.28
First admission	**8.76 (.003)**	**3.24**	**.47**
Eating pathology			
BMI centile	0.28 (.597)	1.21	.08
Purging frequency	0.34 (.561)	2.21	.09
Exercise frequency	0.04 (.835)	0.93	.03
Eating pathology	0.05 (.819)	0.92	.04
Quality of life	0.22 (.637)	0.85	.07
Theoretical variables			
Motivation to recover	0.15 (.704)	1.15	.06
Readiness to recover	0.19 (.666)	1.17	.07
Confidence to recover	0.29 (.593)	0.83	.09
Concern over mistakes	0.26 (.609)	0.84	.08
Personal standards	0.21 (.645)	0.85	.07
Ineffectiveness	0.34 (.562)	1.30	.09
Mood intolerance	0.06 (.802)	1.09	.04
Set-shifting	0.47 (.495)	0.77	.11

Note: results have been adjusted for multiple testing. Significant results are indicated in bold text.

Table 4.3

Baseline predictors and baseline predictors as moderators with time for continuous outcome variables at 3 month follow-up in linear mixed modelling.

	BMI centile		**Eating pathology**		**Quality of life**	
	Variable	Variable x Time	Variable	Variable x Time	Variable	Variable x Time
Predictor	*F (p)*	*F (p)*	*F (p)*	*F (p)*	*F (p)*	*F (p)*
Demographic variables						
Age	0.04 (.851)	1.38 (.265)	0.15 (.699)	2.77 (.084)	0.22 (.642)	1.41 (.265)
Duration	0.01 (.908)	0.38 (.687)	0.74 (.396)	1.13 (.341)	0.01 (.984)	1.28 (.299)
First Admission	0.98 (.328)	0.57 (.572)	0.51 (.478)	0.70 (.506)	1.39 (.247)	0.15 (.859)
Eating pathology						
Admission BMI centile	----------	----------	2.94 (.094)	0.32 (.737)	2.20 (.146)	0.27 (.769)
Purging frequency	0.18 (.671)	0.28 (.754)	**8.06 (.007)**	0.05 (.954)	**9.48 (.004)**	0.46 (.636)
Exercise frequency	0.42 (.519)	**5.00 (.012)**	5.01 (.031)	0.08 (.921)	3.41 (.073)	0.85 (.442)
Eating pathology	0.85 (.364)	2.15 (.131)	----------	----------	**22.92 (<.001)**	0.75 (.485)
Quality of life	0.22 (.640)	1.45 (.249)	**10.49 (.003)**	0.15 (.863)	----------	----------
Theoretical variables						
Motivation to recover	1.16 (.289)	0.27 (.769)	**15.42 (<.001)**	0.23 (.797)	**9.44 (.004)**	1.53 (.242)
Readiness to recover	1.75 (.193)	0.97 (.388)	**10.26 (.003)**	0.68 (.519)	4.87 (.035)	1.02 (.380)
Confidence to recover	2.76 (.105)	0.33 (.722)	5.02 (.031)	1.74 (.202)	2.23 (.144)	1.23 (.314)
Concern over mistakes	0.97 (.330)	0.17 (.844)	**13.89 (.001)**	1.42 (.265)	**16.20 (<.001)**	2.00 (.163)
Personal standards	3.82 (.058)	0.76 (.475)	2.32 (.136)	0.11 (.899)	4.22 (.047)	0.05 (.951)
Ineffectiveness	0.37 (.546)	1.32 (.280)	**21.03 (<.001)**	0.72 (.500)	**16.33 (<.001)**	1.55 (.241)
Mood intolerance	0.02 (.887)	0.63 (.538)	**23.31 (<.001)**	0.61 (.554)	**16.68 (<.001)**	1.75 (.205)
Set-shifting	0.28 (.597)	0.27 (.766)	7.95 (.007)	2.18 (.138)	7.58 (.009)	3.61 (.045)

Note: results have been adjusted for multiple testing. Significant results are indicated in bold text.

Table 4.4

Differences in eating pathology and quality of life scores at each time point for high and low variables emerging as significant in the LMM analyses.

	Admission		Discharge		Follow-up	
	Low	High	Low	High	Low	High
Eating pathology	M (SE)	M (SE)	M (SE)	M (SE)	M (SE)	M (SE)
Purging frequency	3.54 (0.25)[a]	4.78 (0.36)[b]	3.40 (0.29)[a]	4.78 (0.45)[b]	3.12 (0.40)[a]	4.38 (0.62)[b]
Quality of life	3.22 (0.34)[a]	4.67 (0.19)[b]	3.39 (0.24)[a]	4.02 (0.17)[b]	2.80 (0.42)[a]	4.01 (0.28)[b]
Motivation to recover	4.67 (0.28)[a]	3.21 (0.28)[b]	4.66 (0.31)[a]	2.94 (0.31)[b]	4.31 (0.51)[a]	2.80 (0.44)[b]
Readiness to recover	4.59 (0.29)[a]	3.30 (0.29)[b]	4.65 (0.31)[a]	2.70 (0.31)[b]	4.01 (0.50)[a]	3.03 (0.47)[a]
Concern over mistakes	3.38 (0.30)[a]	4.50 (0.30)[b]	3.06 (0.30)[a]	4.64 (0.32)[b]	2.65 (0.44)[a]	4.44 (0.46)[b]
Ineffectiveness	3.16 (0.52)[a]	4.65 (0.51)[b]	3.03 (0.56)[a]	4.52 (0.54)[b]	2.35 (0.62)[a]	4.50 (0.60)[b]
Mood intolerance	3.09 (0.26)[a]	4.79 (0.26)[b]	3.12 (0.34)[a]	4.54 (0.34)[b]	2.44 (0.41)[a]	4.63 (0.44)[b]
Quality of life						
Purging frequency	1.85 (0.11)[a]	2.49 (0.16)[b]	1.75 (0.16)[a]	2.66 (0.26)[b]	1.49 (0.21)[a]	2.14 (0.34)[a]
Eating pathology	1.67 (0.12)[a]	2.45 (0.12)[b]	1.49 (0.16)[a]	2.57 (0.17)[b]	1.29 (0.24)[a]	2.16 (0.25)[b]
Motivation to recover	2.30 (0.14)[a]	1.82 (0.14)[b]	2.48 (0.19)[a]	1.58 (0.18)[b]	2.06 (0.28)[a]	1.40 (0.23)[a]
Concern over mistakes	1.78 (0.13)[a]	2.34 (0.13)[b]	1.56 (0.17)[a]	2.59 (0.18)[b]	1.23 (0.23)[a]	2.20 (0.25)[b]
Ineffectiveness	1.76 (0.42)[a]	2.33 (0.41)[b]	1.58 (0.44)[a]	2.42 (0.44)[b]	1.13 (0.46)[a]	2.21 (0.45)[b]
Mood intolerance	1.74 (0.18)[a]	2.38 (0.28)[b]	1.71 (0.18)[a]	2.40 (0.28)[b]	1.12 (0.28)[a]	2.30 (0.33)[b]

Note: Superscripts indicate where significant differences exist at each time point.

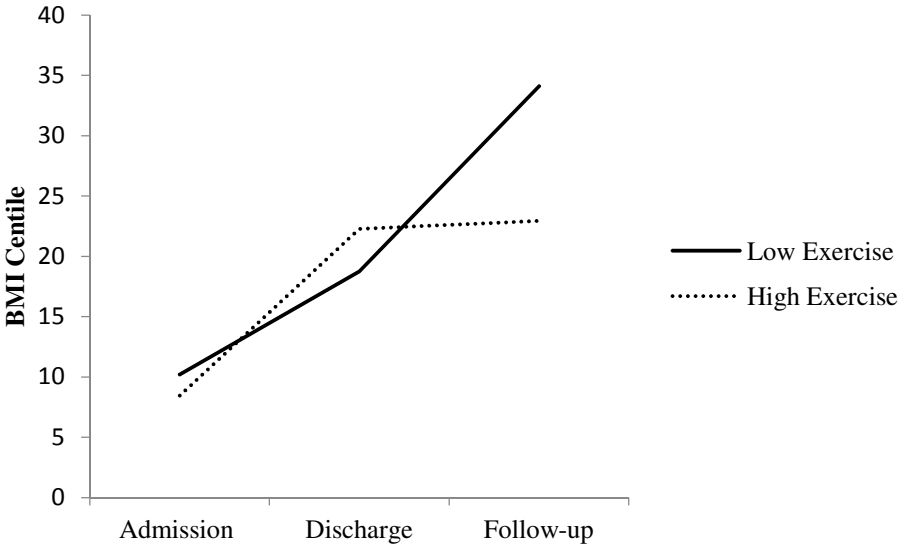

Figure 4.1 Change in BMI centile over time for low and high driven exercise groups.

Chapter 5

Predictors of treatment outcome in a transdiagnostic eating disorder inpatient sample [4]

[4] This chapter was submitted to the *International Journal of Eating Disorders.* Following peer review, a resubmission was invited. The version that appears here incorporates the changes made in response to reviewer feedback. The manuscript has been resubmitted, and at the time of submission of this thesis, was under review.

5.1 Abstract

Objective: We sought to identify theoretically-derived predictors, moderators and mediators of outcome in adults receiving specialist inpatient treatment for an eating disorder.

Method: Consecutive patients (N = 101) were assessed at admission, discharge and 3.5-month follow-up. Outcome variables included change in eating disorder pathology and eating related quality of life (QoL), and for individuals with anorexia nervosa (AN), change in body mass index (BMI). Predictors of drop-out and readmissions during the follow-up period were also investigated. Predictors were selected from prominent theoretical models.

Results: Diagnosis did not predict outcome. Individuals with higher baseline symptom severity exhibited greater symptom improvements at both discharge and follow-up. Those who achieved greater reductions in symptoms during treatment had greater improvements at follow-up. Higher concern over mistakes at baseline predicted greater improvement in symptoms at discharge, but not follow-up. Baseline concerns over mistakes moderated the relationship between improvements in QoL as an inpatient and improvements in QoL at follow-up. For AN, a shorter illness duration and more improvement in QoL during treatment predicted greater gains in BMI by follow-up.

Conclusions: Inpatient treatment allows individuals with severe baseline symptomatology to achieve significant changes that persist after discharge. Robust improvements in eating disorder psychopathology during treatment should be encouraged in order to promote longer-term psychological changes. For individuals with AN, highlighting the improvements that better nutritional health has on broader QoL during treatment may also be important for later weight gain. Future research should continue to examine the predictive value of theoretically informed variables.

5.2 Introduction.

Outcomes for adults with an eating disorder remain sub-optimal even after lengthy periods of treatment (Herzog et al., 1999; Keel & Brown, 2010; Strober et al., 1997). One potential approach to improving outcomes is to identify factors that can predict treatment response. This strategy offers two potential benefits. First, it can identify individuals who are at risk of poor outcome and therefore require additional intervention or prioritised follow-up. Second, it may help to identify potential targets for treatment modifications which could improve efficacy across the population. To date, few robust predictors of outcome have been identified. The most recent review and meta-analysis on the topic (Vall & Wade, 2015a) noted modest evidence to suggest that better outcomes are predicted by greater symptom improvement during treatment, and by various baseline variables including BMI, fewer binge/purge behaviours, greater motivation to recover, lower depression, lower shape/weight concern, fewer comorbidities, better interpersonal functioning and fewer familial problems. However, there was large inter-study variability in effect sizes, disparate operationalisation of outcome, a large range of treatment modalities and different methodologies employed across studies. Accordingly, ongoing research is needed to identify robust and consistent predictors.

One important limitation in the existing literature is the manner in which potential predictors have been selected. Recent reviews have pointed to a general absence of theoretically informed variables (Berkman et al., 2007; Bulik et al., 2007; Steinhausen & Weber, 2009; Vall & Wade, 2015a), which has been indicated as an essential component of treatment research (Craig et al., 2008; Kazdin, 2007). Accordingly, the aim of the current study was to investigate whether consistently indicated theoretical variables would predict treatment outcome. To this end, we selected predictor variables from three prominent theoretical models of disordered eating, namely the Transdiagnostic Model (Fairburn et al., 2003) the Cognitive Interpersonal Model of AN (Schmidt & Treasure, 2006), and the Three-

Factor Model (Bardone-Cone et al., 2006). Shared across these models as maintaining eating disorder symptoms and hindering recovery are high levels of perfectionism/cognitive rigidity, high mood intolerance/emotion avoidance, and low self-efficacy, which is considered to be the active element of self-esteem (Bardone-Cone et al., 2006). To date, there has been limited investigation into the predictive value of these variables for patient outcomes, and they have not been considered together.

There has also been a paucity of investigations of complex predictive processes, in particular treatment moderators and mediators, with the majority of studies exclusively considering simple baseline predictors. While these are important, the inclusion of moderators and mediators is necessary to fully understand the processes influencing outcome (Kraemer et al., 2002). Moderators change the strength of a relationship between two other variables, and help to explain for whom or under what conditions treatment benefits are most likely to be achieved. Mediators explain how or why outcomes are achieved. Kraemer et al. (2008) further specify temporal precedence: a moderator should precede and not be associated with the variable it moderates to predict outcome, while a mediator must follow and be associated with the variable it mediates to predict outcome. The mediator must also be associated with the outcome variable (Kazdin, 2007).

In addition to theoretically informed moderators and mediators of outcome, it is also useful to know whether change in symptoms during treatment might predict later outcomes. While not strictly consistent with the definition of mediation, this nonetheless represents an important process which goes beyond simple baseline prediction, and which is of great clinical interest in the evaluation of treatment predictors. Research in this area to date has focused primarily on change in weight or behavioural symptoms (e.g., purging frequency) during treatment, with only a handful of studies having considered change in psychological

symptoms. In one such study, greater reduction in eating psychopathology early in outpatient treatment led to a higher likelihood of remission for individuals with AN, bulimia nervosa (BN) or other specified feeding and eating disorders (OSFED) (Raykos et al., 2013). For individuals receiving outpatient treatment for BN, change in eating psychopathology at mid-treatment predicted better overall outcomes at end of treatment (Raykos et al., 2014). In a sample of outpatients with BN, early improvements in depressive symptoms predicted remission at both end of treatment and six-month follow-up (Thompson-Brenner, Shingleton, Sauer-Zavala, Richards, & Pratt, 2015). Finally, in a transdiagnostic sample of adults in day or inpatient hospital treatment, decreases in shame led to faster improvements in eating disorder symptoms over the first 12 weeks of treatment (Kelly et al., 2014). Given the limited research into the predictive value of change in psychological variables during treatment, particularly in the inpatient setting, we wanted to examine whether changes in the theoretically indicated variables and in eating disorder psychopathology would predict outcome.

Finally, the majority of existing research has examined predictors for specific eating disorder subtypes, limiting the generalisablity of findings across the eating disorder spectrum. The final aim of the current study was therefore to examine predictors in a transdiagnostic inpatient sample.

In summary, we sought to examine whether variables selected from prominent eating disorder theory would predict, moderate or mediate treatment outcome in a transdiagnostic inpatient sample. We anticipated that higher baseline perfectionism, mood intolerance and ineffectiveness would predict poorer outcomes. We expected that improvements in these variables during treatment, and in eating disorder psychopathology, would be associated with better outcomes at follow-up. Given the absence of existing guidelines about how these

variables might interact to predict outcome, the moderational and mediational analyses were exploratory in nature, and hypothesis generating rather than hypothesis testing.

5.3 Method

5.3.1 Participants and treatment setting.

Participants were consecutive, unique admissions to a specialist inpatient eating disorder unit between September 2013 and August 2015. The unit provides intensive, multidisciplinary, expert care using evidence-based treatments. Briefly, treatment for each individual is determined during pre-admission consultations and reviewed throughout the admission. Treatment modalities common to each individual include nutritional rehabilitation, group and individual psychotherapy (including motivational interviewing and cognitive behaviour therapy), and pharmacotherapy where indicated. Admission criteria included an eating disorder as defined by the DSM-5 (APA, 2013), being at least 15 years of age and medically stable at admission. The admission is intended to be short, where most patients were admitted for around two weeks in order to support them in breaking unhelpful patterns of behaviour and establishing regular eating before discharging them to support in the community. The length of admission was determined based on a combination of target symptoms, predicted treatment response times and patient motivation, and reviewed during the admission based on progress.

5.3.2 Procedure.

The project was approved by the Southern Adelaide Clinical Human Research Ethics Committee. Participants completed the assessment within two days of admission to the ward, and again within the day prior to their discharge. The follow-up assessment was emailed to participants and was completed on average 3.65 months (SD = 1.17) following discharge.

5.3.3 Measures.

Eating pathology.

Eating disorder diagnosis. Eating disorder diagnosis was assigned by the treating team following comprehensive pre-treatment assessment. Diagnoses were assigned based on the criteria set out in the DSM-5 (APA, 2013).

Eating disorder pathology. The self-report Eating Disorder Examination Questionnaire (EDE-Q: Fairburn, Cooper, & O'Connor, 2008) was administered to assess symptom severity. The EDE-Q assesses cognitive and behavioural indicators of eating disorders to yield a global score, where higher scores indicate more severe eating pathology. The EDE-Q has been widely used and validated across studies (Berg et al., 2012). In the present sample, internal consistency was demonstrated with all items correlating with the total scale (average r = .61).

Quality of life. Eating disorder related QoL was measured using the Clinical Impairment Assessment (CIA: Bohn et al., 2008), a 16-item self-report measure. Higher scores indicate higher impairment. The internal validity and test-retest reliability have been demonstrated, and it has been shown to correlate well with the EDE-Q (Reas, Rø, Kapstad, & Lask, 2010). In the present sample, all items correlated with the total scale (average r = .54).

Theoretical predictors.

Perfectionism. Two measures of perfectionism were used, namely the concern over mistakes (CM) and personal standards (PS) subscales from the Frost Multidimensional Perfection Scale (FMPS: Frost et al., 1990). Higher scores indicate greater levels of perfectionism. The scales have demonstrated test-retest reliability (Rice & Dellwo, 2001) and internal reliability (Steele et al., 2011). In the present sample, all items correlated with the total scale for both the CM subscale (average r = .66) and the PS subscale (average r = .68).

***Mood intolerance*.** The 36-item self-report Difficulties in Emotional Regulation Scale (DERS: Gratz & Roemer, 2004) was used, where higher scores indicate more difficulties with emotion regulation, or greater mood intolerance. The DERS has been found to be reliable and valid for use with eating disorder populations (Haynos, Roberto, & Attia, 2015). In the present sample, all items correlated with the total scale (average r = .57).

***Self-efficacy*.** Self-efficacy was measured with the 10-item self-report ineffectiveness subscale of the Eating Disorder Inventory-2 (EDI-I: Garner, 1991) with higher scores indicating greater feelings of inadequacy, insecurity, worthlessness and having no control over one's life. Internal reliability and test-retest consistency of the EDI-I have been demonstrated (Thiel & Paul, 2006). In the present sample, all items correlated with the total scale (average r = .63).

***Cognitive rigidity*.** Set-shifting was used as a measure of cognitive rigidity and was assessed with a freely available electronic version (Mueller & Piper, 2014) of the trail making test (TMT: Reitan, 1955). The TMT has been widely used to study set-shifting in both AN and BN populations (Roberts et al., 2007). Here, set-shifting was indicated by time taken to complete Part B minus time to complete Part A, which has the benefit of controlling for motor speed. People with BN have shown significantly sub-optimal performance compared to controls (Vall & Wade, 2015b).

5.3.4 Analytic strategy.

Primary patient outcomes. The outcome variables were change in eating disorder pathology and QoL, and for patients with AN, change in BMI, at end of treatment and at follow-up. Drop-out and readmission were examined as secondary outcome measures. Drop-out was defined as discharge prior to completing at least 75 per cent of the planned treatment

program. Readmission was defined as a psychiatric admission of at least one night to any of the public hospitals in South Australia.

Missing data. Missing data were imputed using the *expectation–maximization (EM)* algorithm. Data were first examined to determine whether data were missing at random (MAR), or whether there were distinct patterns of missingness. No baseline variables predicted missingness, with the exception of age (Wald = 5.56, $p = .018$) and duration of illness (Wald = 5.19, $p = .023$), with those who had an older age or longer duration being more likely to have a complete data set. Little's (Little, 1988) tests suggested that data were MAR for each variable where data was to be imputed.

Statistical analyses.

To determine whether there were significant improvements between the three time points, linear mixed modelling was conducted for each of the outcome variables (eating pathology, QoL and for AN only, BMI).

***Simple predictors*.** To examine the relationships between the baseline theoretical predictor variables and outcome variables, baseline variables that showed a significant correlation ($p < .05$) with change in the dependent variables to discharge or follow-up were then entered into a multivariate regression to determine which retained significant associations with outcome. To examine differences in outcomes between individuals scoring high and low on significant baseline predictors, a median split on the predictor was performed.

Change in variables during treatment as predictors. To determine whether change in any baseline variable during treatment predicted change in outcome to follow-up, a change score for each potential predictor variable was calculated between admission and discharge. Change scores that showed a significant correlation with follow-up outcome were then entered into a multivariate regression to determine which retained significant associations.

Moderators and mediators of change in outcome variables to follow-up. As three time points are needed for strictly defined analyses of moderators and mediators of outcome (Kraemer et al., 2008), these analyses were only conducted for the follow-up outcome. The intermediate variable (i.e., occurring between baseline and follow-up) was change in the relevant outcome variable at discharge (where this change proved to be a significant predictor of follow-up outcome). Theoretical baseline predictor variables that were not correlated with change to end of treatment were considered as potential moderators, while those that were correlated with change to end of treatment were conceptualised as potential mediators (Kazdin, 2007; Kraemer et al., 2008). To prepare the data for regression analyses, all predictor variables were centred so that the mean was equal to zero, and interaction terms were computed. In the first step of the linear regression, predictor variables were entered. In the second step, the interaction term was added.

Change in BMI for AN only. A second set of analyses were conducted for the AN subsample to examine predictors of change in BMI. The same procedures were followed as described above.

Magnitude of effects. The correlation coefficient, r, was calculated as a measure of effect size, where r = .10 constitutes a small effect, r = .30 a medium effect, and r = .50 a large effect (Cohen, 1992), and 95 per cent confidence intervals were also calculated.

5.4 Results

5.4.1 Patient characteristics.

Our sample consisted of 101 individuals. Descriptive statistics are shown in **Table 5.1.** Almost half the sample (44.6 %) were first-time presentations for inpatient treatment, with the remainder having at least one prior admission. AN-restrictive subtype was the most common diagnosis (41.6 %), followed by BN (28.7%), AN-binge/purge subtype (15.8%) and OSFED

(13.9%). The sample was predominantly female (n = 98, 97%) and Caucasian (n = 96, 95%). A flow diagram showing attrition at each of the three time points is given in **Figure 5.1.**

5.4.2 Key outcome variables.

There were significant improvements in BMI, eating disorder pathology and QoL between admission and discharge, as shown in **Table 5.2**. Between discharge and follow-up, there were further significant improvements for BMI, and gains in QoL were maintained, while eating disorder pathology increased significantly, whilst still being significantly lower than baseline levels. The total drop-out rate was 22.8% (n = 23). Drop-outs and treatment completers did not differ on any baseline variable, or on any outcome variables at follow-up. During the follow-up period, 28.7% of the sample (n = 29) were readmitted at least once.

5.4.3 Predicting change in outcome variables for the whole sample.

The correlations between all the baseline predictor variables, change in outcome variables at the different time points and change in predictor variables during treatment are given in **Table 5.3.**

Predictors of drop-out and readmission. There were no baseline predictors of drop-out or readmission.

Predictors of change in outcome variables between admission and discharge.

Eating pathology. There were six univariate baseline predictors of greater improvement in eating pathology at discharge; higher eating pathology, concern over mistakes, personal standards, difficulties with emotion regulation and ineffectiveness, and lower QoL. In a multivariate analysis, baseline eating pathology was the only significant predictor (t = -6.84, p <.001, r = -.57, 95% CI = -.69:-.42). Individuals with higher disordered eating at baseline exhibited greater improvement in eating pathology during treatment, as shown in **Table 5.4.** Baseline concern over mistakes was also approaching significance in the

multivariate analysis (t = 1.97, p .052, r = .19, 95% CI = -.00:.38). Those with higher concern over mistakes at baseline had greater improvement in eating pathology by discharge.

Quality of life. There were two univariate baseline predictors of greater improvement in QoL, namely higher eating pathology and lower QoL. Only baseline QoL survived in the multivariate analysis (t = -4.14, p <.001, r = -.38, 95% CI = -.54:-.20). Individuals with lower QoL at baseline exhibited greater improvements in QoL during treatment, as shown in **Table 5.4**.

Predictors of change in outcome variables between admission and follow-up.

Eating pathology. There were five univariate baseline predictors of greater improvement in eating pathology at follow-up; higher eating pathology, lower QoL, lower personal standards, greater change in eating pathology between admission and discharge and greater change in QoL between admission and discharge. In a multivariate analysis, baseline eating pathology was the only significant predictor (t = -2.28, p = .025, r = -.22, 95% CI = -.40:-.03). Individuals with higher disordered eating at baseline exhibited greater improvements in eating pathology between admission and follow-up, as shown in **Table 5.4**.

Quality of life. There were five univariate predictors of change in QoL to follow-up; namely baseline QoL and mood intolerance, and change at discharge in eating pathology, QoL and mood intolerance. After including all of these in the multivariate analysis, only change in QoL at discharge retained significance (t = 3.28, p = .001, r = .31, 95% CI = .13:.48). Individuals who achieved greater improvements in QoL by discharge had greater improvements in QoL at follow-up.

Mediators of change in disordered eating to discharge to predict change in disordered eating between admission and follow-up.

Eating pathology. As there were no predictors of change in eating pathology to follow-up at our second time-point (discharge), no mediator analyses could be conducted.

Quality of life. While change in QoL between admission and discharge was a significant predictor of change at follow-up, none of the theoretical baseline variables was correlated with change to discharge, so no mediator analyses could be conducted.

Moderators of change in outcome variables between admission and discharge to predict change between admission and follow-up.

Eating pathology. The only theoretical baseline variable that was not correlated with change in eating pathology between admission and discharge was set-shifting. There was no main effect of set shifting ($t = 0.32$, $p = .789$) and no interaction between set-shifting and change to discharge ($t = 0.52$, $p = .795$) on follow-up outcome.

Quality of life. As none of the theoretical baseline variables were correlated with change in QoL between admission and discharge, they were all considered as potential moderators of the change in QoL to follow-up. The results of the regressions for each of these models is shown in **Table 5.5.** The model with concern over mistakes was significant. As shown in **Figure 5.2,** post-hoc testing revealed that those individuals who exhibited greater improvements in QoL to discharge and who had lower concern over mistakes at baseline, achieved the greatest improvements in QoL between admission and follow-up. However, the magnitude of this difference was small ($r = .06$, 95% CI = -.14:.25).

5.4.4 Predicting change in BMI for the AN subsample only.

Predictors of change in BMI between admission and discharge. There were no baseline predictors of change in BMI between admission and discharge.

Predictors of change in BMI between admission and follow-up. There were three univariate predictors of change in BMI between admission and follow-up, namely mood intolerance and duration, plus change in QoL to discharge. In the multivariate analysis, both duration (t = -2.67, p = .011, r = -.34, 95% CI = -.55:-.09) and change in QoL (t = -2.69, p = .011, r = -.34, 95% CI = -.55:-.09) retained significance. Post-hoc testing revealed that individuals with a longer duration exhibited less improvements in BMI between admission and follow-up compared to those with a shorter duration. Individuals who had greater improvements in QoL during treatment, gained more weight between admission and follow-up.

Moderators and mediators of change in BMI. As one time two variable was significantly correlated with change in BMI to end follow-up, namely change in QoL at discharge, it was possible to consider theoretical baseline mediators and moderators of this effect. As none of the theoretical baseline variable was correlated with change in QoL to discharge, no mediator analyses could be conducted. None of the moderator models yielded significant interactions.

5.5 Discussion

The aim of this study was to identify theoretically-informed predictors, moderators and mediators of outcome in a transdiagnostic inpatient sample. Diagnosis did not predict outcome, lending support to the transdiagnostic view of eating disorders (Fairburn et al., 2003; Waller, 2008), which to date has been largely advanced within outpatient treatment modalities (Fairburn et al., 2015; Fairburn et al., 2009; Loeb, Lock, Greif, & le Grange, 2012). Our results suggest that patients may also benefit from intensive, psychologically-focused inpatient treatment irrespective of diagnosis.

Our first finding was that improvements in eating pathology and QoL during treatment were predicted by more severe respective baseline levels of these constructs. This seems to

contradict studies that have reported that baseline symptom severity is associated with poorer outcomes (Vall & Wade, 2015a). However, most studies have considered binary outcome measures (e.g., recovered versus not recovered) or static outcomes measured at a single point in time (e.g., disordered eating at follow-up). By contrast, we were interested in change in symptoms as an outcome. Accordingly, the current results are feasible, because individuals with a higher baseline severity, given the right treatment conditions, theoretically have greater scope to evidence decreases in symptoms. However, two points should be considered in the interpretation of this result. First, although the magnitude of improvement was larger for those with higher baseline severity, they nonetheless exhibited higher symptoms at all time points. Accordingly, ensuring that symptom improvement continues in the longer term for these individuals will be important. Second, individuals with less severe symptoms at baseline made much smaller gains, and may therefore need additional encouragement or intervention to ensure that satisfactory progress is achieved. Alternatively, less intensive treatments may be preferably indicated for these individuals.

Our second main finding was that greater improvement in QoL during treatment predicted greater overall improvement in QoL by follow-up, consistent with previous research with outpatient samples (Lock et al., 2013; Raykos et al., 2014). Additionally, for individuals with AN, improvement in QoL during treatment predicted greater weight gain at follow-up. This finding might be explained by the value that individuals with an eating disorder place on their symptoms, often to the exclusion of other life domains, helping to maintain the disorder (Schmidt & Treasure, 2006). It is plausible therefore that improvements in general QoL serve to diminish the perceived benefits of the eating disorder, giving way for behavioural change such as weight gain, as seen in the current study. From a clinical point of view, psychological treatment might need to focus more heavily on highlighting the improvements across the

various domains of life, in addition to addressing the maladaptive beliefs about the function of the eating disorder.

Interestingly, improvements in eating psychopathology during treatment did not have the same predictive effect as changes in QoL. This is surprising given that change in eating pathology did predict better long-term outcomes in outpatient settings (Raykos et al., 2013). This might reflect the contained nature of the inpatient setting in which patients are forced to abandon eating disorder behaviours (purging, exercise, restriction), leading to positive changes in eating psychopathology during the course of treatment. When this containment is removed post-discharge, disordered behaviours are free to resume, possibly resulting in a spike in associated psychopathology and more limited improvements at follow-up. In intensive inpatient settings, ensuring that sufficient post-discharge supports are in place to prevent rapid symptom escalation will be important to prevent this pattern.

Our third main finding suggests that, although the theoretical variables were related to outcomes at discharge, contrary to our expectations, they did not hold their predictive value once severity of eating pathology and QoL were included in the analyses, nor did they predict outcomes at follow-up. One explanation for this is that our sample was underpowered to detect these effects in the multivariate analyses. It may also be explained by the short and intensive nature of the treatment, which focused primarily on improving eating disorder symptoms and psychopathology. The more limited therapeutic focus on addressing maintaining variables may have meant that there was insufficient change in the theoretical variables for predictive effects to occur. Future research should continue to examine these variables in different treatment settings and with larger samples. One exception to this general trend was the moderation of concern over mistakes on the relationship between change in QoL over treatment and change in QoL at follow-up. It may be those with lower levels of self-critical

perfectionism found it less threatening to experiment with change as an inpatient, which produced benefit for QoL over treatment and consequently at follow-up. This suggests that greater support to test unhelpful beliefs as an inpatient might result in benefits to the patient. There is some evidence to support this. In one study of inpatients with AN, exposure therapy to confront fear and anxiety around eating resulted in improvements in dietary intake and eating related anxiety (Steinglass et al., 2014). Further examination of supported behavioural experiments as useful enhancements to existing protocols deserves further consideration.

When interpreting the current results, several limitations warrant discussion. First, the research took place within a naturalistic treatment setting. While the treatment principles were the same and there was much overlap in protocol, it cannot be guaranteed that all patients received exactly the same treatment. Second, as our follow-up period of approximately 3.5 months was quite short, we do not know if the reported effects persisted in the longer-term. Third, our sample size of 101 may have lacked power to detect some effects. Finally, we did not have data about patients' engagement with outpatient treatment and/or supports after discharge, which may have impacted on post-discharge symptom change.

In conclusion, the current findings suggest that individuals with more severe eating psychopathology at baseline are likely to respond robustly to inpatient treatment. A clinical focus on improving and highlighting changes to broader QoL during treatment may help in achieving better outcomes in the longer term. Ongoing research is needed to determine the extent to which theoretical variables have predictive value in inpatient treatments.

Table 5.1

Descriptive statistics for baseline variables. Values are given as M(SD) for continuous variables and N (%) for categorical variables

Variable	Baseline
Age (years)	24.27 (7.40)
Duration (years)	8.39 (7.67)
Diagnosis	AN = 58, BN/OSFED = 43
Length of stay (days)	16.52 (12.17)
Drop-out	23 (22.8%)
Readmission	29 (28.7%)
Eating pathology (EDE-Q)	4.53 (1.18)
Quality of life (CIA)	2.43 (0.46)
Concern over mistakes	3.90 (0.73)
Personal standards	3.80 (0.80)
Difficulties with emotion regulation	3.67 (0.71)
Ineffectiveness	1.77 (0.75)
Set-shifting (Trail Making Test)	33.95 (25.16)
Change in EDE-Q score to discharge	-1.00 (0.98)
Change in EDE-Q score to follow-up	-0.62 (1.24)
Change in QoL score to discharge	-0.35 (0.48)
Change in QoL score to follow-up	-0.38 (0.70)

Note: EDE-Q = Eating Disorder Examination – Questionnaire, CIA = Clinical Impairment Questionnaire

Table 5.2

Significant interactions in linear mixed models between time and change in dependent variables between baseline and follow-up, by group, with effect sizes between each time point.

		T1	ES (T1-T2)	T2	ES (T2-T3)	T3		ES (T1-T3)
	N	M (SE)	*r*	M (SE)	*r*	M (SE)	*F (p)*	*r*
BMI[1]	58	15.92 (1.53)[a]	.19	16.56 (1.71)[b]	.11	16.97 (2.02)[c]	**22.55 (<.001)**	.28
Eating pathology	101	4.53 (1.18)[a]	.43	3.53 (0.92)[b]	.17	3.92 (1.27)[c]	**39.31 (<.001)**	.24
Quality of life	101	2.43 (0.46)[a]	.35	2.07 (0.50)[b]	.02	2.05 (0.68)[b]	**18.39 (<.001)**	.31

[1]Only cases with a BMI < 18.5 included in these analyses. ES = effect size, T1 = baseline, T2 = discharge, T3 = follow-up. Superscripts indicate significant differences between values at different time points. Significant results are indicated in bold text.

Table 5.3

Correlations between all baseline variables and change in outcome variables.

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1	Duration (years)	---																
2	Diagnosis	**-.23**	---															
3	Drop-out	ns	ns	---														
4	Readmission	ns	ns	ns	---													
5	EDE-Q	ns	**.21**	ns	ns	---												
6	QoL	ns	ns	ns	ns	**.66**	---											
7	CM	ns	ns	ns	ns	**.51**	**.50**	---										
8	PS	ns	ns	ns	ns	**.21**	ns	**.46**	---									
9	DERS	ns	**.26**	ns	ns	**.43**	**.60**	**.47**	ns	---								
10	Ineffectiveness	ns	**.20**	ns	ns	**.52**	**.63**	**.54**	ns	**-.68**	---							
11	Set-shifting	**.21**	ns	ns	ns	ns	ns	ns	ns	ns	ns	---						
12	ΔEDE-Q - discharge	ns	ns	ns	ns	**-.65**	**-.40**	**-.22**	**-.22**	**-.23**	**-.24**	ns	---					
13	ΔEDE-Q– follow-up	ns	ns	ns	ns	**-.45**	**-.28**	ns	**-.21**	ns	ns	ns	**.39**	---				
14	ΔQoL - discharge	ns	ns	ns	ns	**-.23**	**-.43**	ns	ns	ns	ns	ns	**.58**	ns	---			
15	ΔQoL– follow-up	ns	ns	ns	ns	ns	**-.37**	ns	ns	**-.20**	ns	ns	**.20**	**.68**	**.42**	---		
16	Baseline BMI[1]	ns	---	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	---	
17	ΔBMI – discharge[1]	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	ns	---
18	ΔBMI – follow-up[1]	**-.38**	ns	ns	ns	ns	ns	ns	ns	**-.30**	ns	ns	ns	ns	**-.31**	ns	ns	ns

Note: All reported correlations are significant at $p < .05$. ns = not significant, EDE-Q = Eating Disorder Examination – Questionnaire, QoL = quality of life, CM = concern over mistakes, PS = personal standards, DERS = Difficulty with Emotional Regulation Scale, [1] Only cases with AN diagnosis included in these correlations

Table 5.4

Outcome variables at each time point for individuals with high and low baseline levels of the outcome variable, and differences between high and low groups at each time point.

	Baseline			Discharge			Follow-up		
	Low M(SD)	High M(SD)	*t (p)*	Low M(SD)	High M(SD)	*t (p)*	Low M(SD)	High M(SD)	*t (p)*
Eating pathology	3.66 (1.10)	5.39 (0.27)	10.87 (<.001)	3.13 (0.88)	3.91 (0.80)	4.69 (<.001)	3.25 (1.25)	4.57 (0.92)	6.06 (<.001)
Quality of life	2.11 (0.41)	2.78 (0.16)	10.73 (<.001)	1.91 (0.50)	2.25 (0.43)	3.58 (.001)	1.86 (0.67)	2.25 (0.65)	2.95 (.004)

Table 5.5

Moderational interactions between theoretical baseline predictor variables and change in quality of life (QoL) between baseline and discharge, predicting change in QoL between baseline and follow-up.

Model	*t*	*p*	*r*	95% CI
Personal standards, Δ QoL				
Univariate main effects				
Personal standards	-0.60	.550	-.06	-.25 : .14
Δ QoL	**4.48**	**<.001**	**.41**	**.24 : .56**
Two- way interactions				
Personal standards x Δ QoL	-1.06	.294	-.11	-.30 : .09
Concern over mistakes, Δ QoL				
Univariate main effects				
Concern over mistakes	-0.54	.587	-.05	-.25 : .14
Δ QoL	**4.42**	**<.001**	**.41**	**.23 : .56**
Two- way interactions				
Concern over mistakes x Δ QoL	**-2.66**	**.009**	**-.26**	**-.43 : -.07**
Ineffectiveness, Δ QoL				
Univariate main effects				
Ineffectiveness	-0.43	.665	-.04	-.24 : .15
Δ QoL	**4.27**	**<.001**	**.39**	**.22 : .55**
Two- way interactions				
Ineffectiveness x Δ QoL	-0.92	.359	-.09	-.28 : .11
Mood intolerance, Δ QoL				
Univariate main effects				
Mood intolerance	-1.39	.168	-.14	-.33 : .06
Δ QoL	**4.27**	**<.001**	**.39**	**.22 : .55**
Two- way interactions				
Mood intolerance x Δ QoL	-0.28	.777	-.03	-.23 : .17
Set-shifting, Δ QoL				
Univariate main effects				
Set-shifting	-0.21	836	-.22	-.22 : .18
Δ QoL	**4.11**	**<.001**	**.38**	**.20 : .54**
Two- way interactions				
Set-shifting x Δ QoL	-0.81	422	-.08	-.27 : .12

Note: Significant results are indicated in bold text. QoL = quality of life

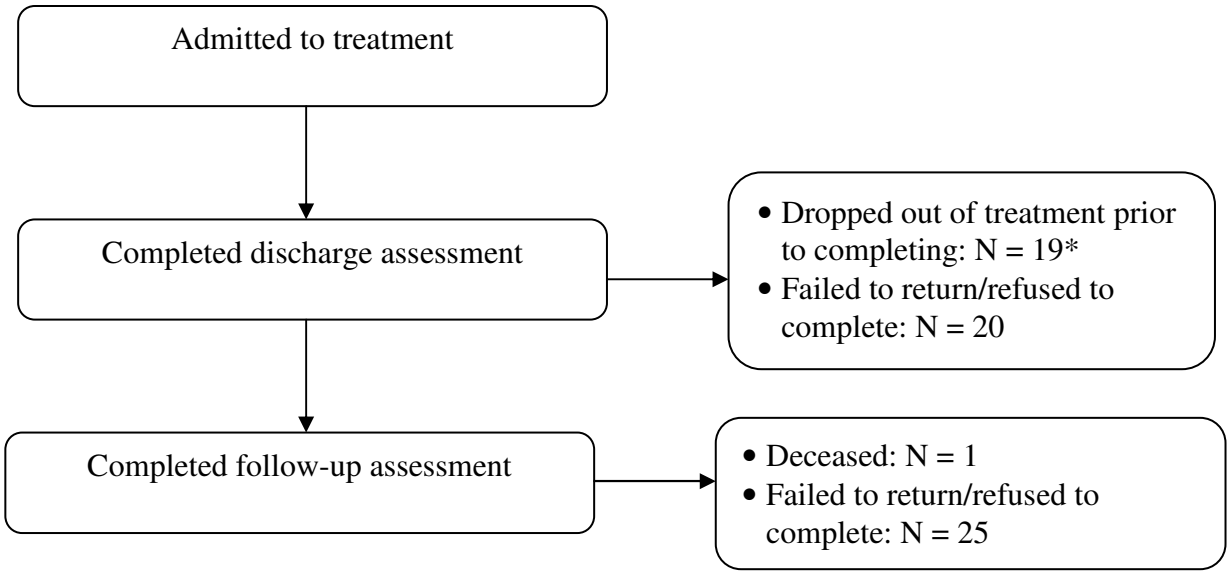

Figure 5.1 Flow diagram indicating attrition at each time point.

*The total treatment drop-out was N = 23, but four patients completed the assessment despite their early discharge

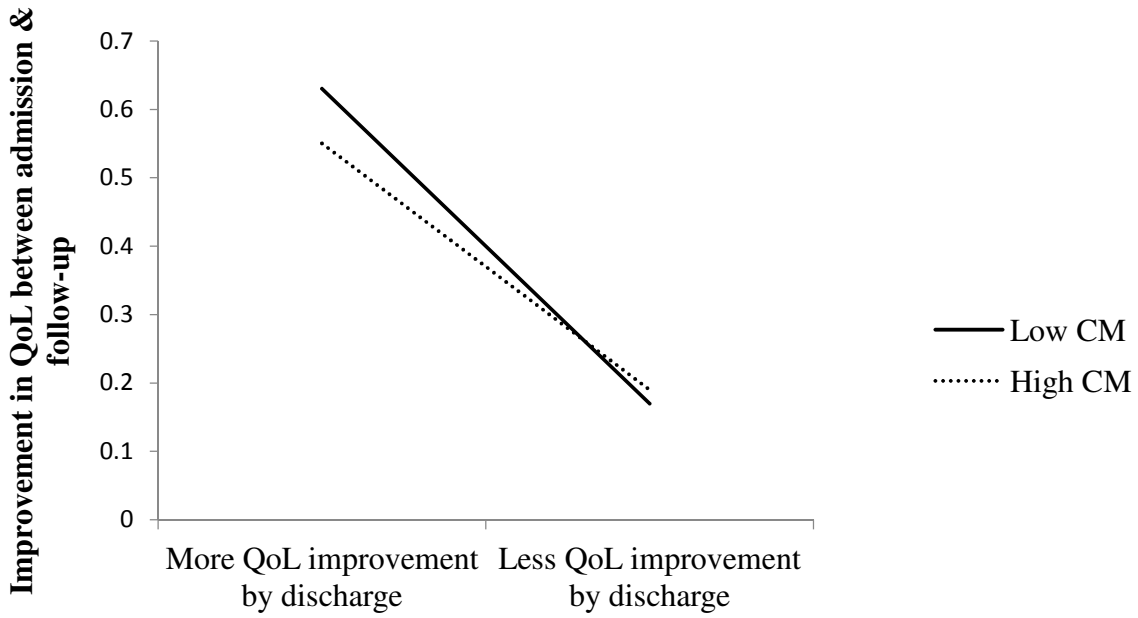

Figure 5.2 Improvement in QoL scores between admission and follow-up for combinations of high and low baseline concern over mistakes, and high and low improvement in QoL scores to discharge. Note that a higher score signifies greater improvement. QoL = quality of life, CM = concern over mistakes

Chapter 6

General Discussion

6.1 Overview

The purpose of the following discussion is to integrate the findings from the four studies conducted in this thesis, thereby presenting its overall contribution to this field of research. Throughout, methodological limitations are discussed, clinical and theoretical implications of the research are highlighted, and directions for future research are suggested.

6.2 Summary of the Present Research

This thesis sought to contribute to, and improve, the current understanding around predicting outcomes in individuals receiving treatment for an eating disorder. It aimed to do so by identifying the key limitations that have hindered progress in the area, and addressing these through empirical studies that examined predictors of outcomes in an adult and an adolescent clinical sample. This is an important area of enquiry, as treatment response for eating disorders continues to be sub-optimal across diagnoses, age-groups and treatment modalities. Without a thorough understanding of what predicts treatment response, our ability to ameliorate this state of affairs is hindered. Such insights can provide important prognostic information at the individual level, and may also highlight targets for treatment modifications that might improve outcomes across broader patient sub-groups.

The systematic review and meta-analysis conducted for this thesis revealed that although the topic has been frequently considered in previous research, limitations in the way it has been approached have resulted in substantial inconsistencies and weaknesses in the existing knowledge base. Most notably, the existing literature base included very few theoretically informed, statistically complex analyses, little consideration of transdiagnostic predictors, and a vast array of different measures of outcome. The recommendations provided in the meta-analysis for addressing these limitations subsequently guided the development of the empirical studies. Accordingly, the present results not only provide additional insights into

specific potential predictors of outcome, they also contribute to the development of a more fruitful approach to the identification of predictors in the future.

6.3 Integration of Key Findings and Clinical Implications

6.3.1 Predictive value of the theoretical variables.

Although the individual theoretical variables indicated in the current research, namely perfectionism, mood intolerance and self-efficacy, were clearly associated with illness severity at all stages in the adolescent sample, their contribution as predictors of outcome over time in the adolescent sample was limited. Their predictive value in the adult sample was similarly limited. One explanation for the lack of robust theoretical findings is that the treatment settings were not the most appropriate for testing theoretical predictors. The nature of the inpatient setting means that the samples may have represented a more acutely unwell demographic, for whom swift and targeted eating disorder symptom improvement was the primary focus. In this context, the theoretical predictors may well have been important, but simply overshadowed by the magnitude of the effects related to symptom severity and symptom change. Another potential problem with conducting this kind of research in the naturalistic setting is that although the treatments were evidence-based, they were nonetheless delivered in a treatment-as-usual setting, and therefore it was not possible to control the individual treatment components or processes across patients. In this setting, while treatment for all patients would undoubtedly have focused on eating disorder symptom and psychopathology reduction, the degree to which other maintaining factors were addressed or altered may have varied. Finally, the current guidelines from the Medical Research Council (Craig et al., 2008) highlight the importance of drawing from relevant theory when developing, and most importantly, when evaluating, treatment interventions. This is considered important in order to identify the relevant causal mechanisms so that interventions (and the theory that drives them), can be continually improved. However, the guidelines

suggest that randomized trials are the preferred method for conducting such evaluations, particularly where there is interest in identifying variables that contribute outcome. Another potential explanation for the lack of robust predictive effects that must be considered is a genuine non-association between the variables. Most research to date has considered single variables as predictors, with little examination of interactions between variables, particularly theoretically-informed interactions. This is an important area of future enquiry that is essential to better determine the robustness of existing models, and to inform modifications that will render them more accurate. To this end, the inclusion and analysis of theoretical variables in future controlled treatment trials in the eating disorder field would be of great value to improving our understanding of the theoretical maintenance models, and the value of these models in understanding patient outcomes.

Nonetheless, the present results did provide some support for the selected theoretical variables. In particular, concern over mistakes perfectionism emerged as important both in terms of illness severity at all time points in the adolescent sample, and in the adult sample as a potentially important predictor and moderator of outcome. Increase in personal standards during treatment predicted readmission for adolescents. While further research is needed to better understand these effects, the fact that perfectionism was indicated across both samples suggests that such research is indeed warranted. From a clinical perspective, the present results suggest that interventions that target perfectionism may be valuable both in improving eating pathology and quality of life at all stages of illness, as well as potentially improving treatment outcomes. There is evidence that perfectionism is modifiable (Lloyd et al., 2014; Shafran, Lee, Payne, & Fairburn, 2006), and that it is lower in individuals who have recovered from an eating disorder, compared to those who are currently ill or in recovery (Bardone-Cone, Sturm, Lawson, Robinson, & Smith, 2010). It is therefore surprising that there has been relatively little investigation into the treatment of perfectionism in individuals with an eating disorder.

Enhanced cognitive behaviour therapy for eating disorders (CBT-E: Fairburn, 2008) has the optional inclusion of a module addressing maladaptive perfectionism in its 'broad' form, but this is usually reserved for individuals who present with marked perfectionistic features (Murphy, Straebler, Cooper, & Fairburn, 2010). A guided self-help (GSH) treatment based on cognitive behaviour therapy for perfectionism was equally effective in reducing bulimic symptoms as GSH based on CBT-E and as a mindfulness-based placebo GSH treatment (Steele & Wade, 2008). However, the small sample size in that study was identified as a potential barrier to detecting significant differences between groups. Finally, there has been a recent suggestion that adding interventions around perfectionism to established eating disorder treatments such as family based treatment for adolescent AN may enhance their effectiveness (Hurst & Zimmer-Gembeck, 2015), but this study included several cases only. It is unclear therefore whether the routine addition of perfectionism interventions to eating disorder treatments on a larger scale might usefully enhance outcomes. Intervention studies involving greater numbers of patients will be an important target for future research in order to clarify whether the targeting of perfectionism might improve treatment outcomes.

However, it should be noted that interventions that seek to target multi-faceted perfectionism may not be effective across all groups. There are two reasons for this. First, the present results suggest that personal standards and concern over mistakes represent separate kinds of construct. Unlike concern over mistakes perfectionism, personal standards perfectionism was not strongly correlated with the other theoretical predictor variables (mood intolerance, self-efficacy). Second, the measures of perfectionism behaved differently with different patient groups. For example, in the adolescent sample, change in personal standards during treatment predicted follow-up outcome, while in the adult sample personal standards had no relationship with outcomes. It is difficult to know whether the different results obtained in the two samples with respect to personal standards are to be expected, as there has been

little research that has compared perfectionism across age groups within the eating disorder literature. There is some evidence that vomiting might be associated with lower levels of personal standards (Reba et al., 2005), which might have reduced the impact of this measure within the adult sample given the inclusion of patients with BN and the higher proportion of binge/purge subtype of AN. One study also found that adults with AN or BN did not have elevated scores compared to controls on measures that are broadly similar to the personal standards construct (Waller et al., 2012). Concern over mistakes perfectionism, on the other hand, appears to feature equally across subtypes and presentations (Bardone-Cone et al., 2007), which might explain its emergence as important in both the samples studies in the present research. The distinction between the two types of perfectionism considered in the present research is potentially important in the implementation of interventions, as broad treatments aimed to address all facets of the construct may be inefficient. Instead, interventions that address the perfectionism constructs separately and target particular sub-groups (e.g., adults versus adolescents) are likely to be most effective.

6.3.2 Change in eating disorder symptoms and psychopathology during treatment.

A main finding of the present research was that in both the adult and adolescent samples, individuals who achieved greater symptom improvement during treatment had better outcomes at follow-up. This reinforces the finding in the meta-analysis that showed symptom change during treatment as one of the few robust predictors of outcome across a range of diagnoses and treatment settings. One explanation for this effect is that improvements in symptoms during treatment may in fact reflect an overall improvement in motivation, which subsequently persisted post-discharge, leading to the ongoing improvements that were present at follow-up. This is consistent with Waller's (2012) assertion that behavioural change is the most tangible representation of motivation in the eating disorders, and given that interventions

designed to enhance motivation have been largely unsuccessful (Knowles et al., 2013), focusing on driving symptom changes during treatment deserves ongoing consideration as an important therapeutic goal.

Taken together, the findings around symptom change and better outcomes support the notion that driving symptom change should be a central focus during treatment, with weight change an important target for intensive inpatient adolescent treatment, and psychological change important for intensive psychologically focused inpatient treatment for adults. This might also provide some direction for clinicians when considering discharge planning, particularly in the case of treatments as usual where there is not always a specified treatment duration or number of sessions. Appropriate action may require earlier discharge where there is little change, in favour of trying an alternative approach. Alternatively it may mean that more assertive follow-up and monitoring is offered in order to offer short, intermittent treatments that can minimize physical harm but not lead the patient to conclude that the treatment has been tried but failed. Using information about the importance of early change with the patient may also motivate them to make the most of their treatment in the early days. Defining a sufficient versus an insufficient level of symptom change during treatment does however pose some challenges, as such a definition will depend on the treatment setting, the outcome of interest, and the symptoms that are being targeted in treatment. For example, a 50 per cent reduction in binge frequency by the third session in individuals with BN or BED receiving guided self-help treatment was strongly predictive of remission at six-month follow-up (Vaz, Conceição, & Machado, 2014), while in adult inpatients with AN, the number of weeks taken to gain two thirds of a pre-set target weight was most predictive of discharge BMI (Mewes, Tagay, & Senf, 2008). Rather than a specific target or cut-off point, the majority of studies have reported that greater overall improvement in a symptom of interest predicted

outcome. Applying sound clinical judgment and knowledge of the treatment sample and setting is therefore crucial to effectively translate these findings into useful clinical practice.

There were however some interesting differences between the adult and adolescent samples in the present research. First, change in BMI during treatment predicted later weight outcomes for adolescents only. This may simply reflect the difference in the nature of treatment goals across the two settings, in that weight restoration was a more prominent focus in the adolescent treatment program, and therefore a greater magnitude of weight change was evident in the younger sample. Second, the fact that change in psychological eating pathology factors during treatment (eating pathology and quality of life) predicted better psychological outcomes for adults, but not adolescents, might simply reflect the more psychological focus of the treatment program, and the greater changes in these domains within the adult sample. Moreover, the finding related to increased quality of life predicting greater increase in BMI over time in the adult sample was both unexpected and novel, and suggests that therapeutic focus on this domain for adult inpatients may be an important treatment goal.

6.3.3 Change in theoretically indicated variables during treatment.

Another important finding was that in addition to change in eating disorder symptoms and psychopathology, change in several of the theoretical variables during treatment also predicted outcome. For adolescents, increased personal standards perfectionism was associated with greater likelihood of readmission, while for adults, an increase in mood intolerance during treatment predicted poorer quality of life at follow-up (although this effect was not significant in the multivariate analysis). These results are important, because to date very few studies have identified change processes involving psychological maintaining factors, focusing instead on eating disorder specific symptomatology. These change processes deserve ongoing investigation as potentially modifiable treatment targets that could improve overall treatment success rates. As already discussed, perfectionism is potentially modifiable

in therapeutic settings, but there is far less research describing treatments that target mood intolerance. Prominent cognitive-behavioural interventions include optional modules that address mood intolerance (Fairburn, 2008), and outpatients with marked mood intolerance appear to benefit more from these than patients with less complex psychopathology (Fairburn et al., 2009). It would be valuable to evaluate interventions with a mood intolerance focus across different treatment settings and with more diverse patient groups. In particular, interventions that focus on reducing affect avoidance and building emotional management skills have been highlighted as important targets (Corstorphine, Mountford, Tomlinson, Waller, & Meyer, 2007).

6.3.4 Set-shifting.

While the validation of the measure of a theoretically important variable, set-shifting, showed that it is appropriate for use with inpatient eating disorder populations, the measure was not a strong predictor of outcome in either of the two empirical studies, particularly in the adult sample. In the validation sample, individuals with AN did not show impaired performance on the measure compared to healthy controls, while those with BN exhibited clear deficits. Given that AN was the primary diagnosis in the two inpatient studies, set-shifting deficits within the sample may have been too minimal to have any effect on outcomes. There is some evidence that illness severity is linked to poorer performance on set-shifting measures in individuals with AN (Tchanturia et al., 2004), and further examination of this measure in a medically unstable adult sample may provide important insights into how it relates to outcome depending on stage of physical recovery. Given that set-shifting in the adolescent population was approaching significance for several outcome measures, this might indicate that the measure is of greater utility in a more medically unstable group. However previous research comparing adolescent inpatients with AN and healthy controls showed no differences on set-shifting measures (Fitzpatrick, Darcy, Colborn, Gudorf, & Lock, 2012),

although the TMT was not one of the measures administered. A review of set-shifting in adolescents with AN that included several studies that employed the TMT concluded that unlike adults with AN, adolescents may not exhibit deficits in set-shifting (Lang et al., 2014).

On the other hand, set-shifting within adults with BN may represent an important but understudied area. Given that adults with BN in our validation study exhibited marked deficits in set-shifting compared to the control group, it would be valuable to examine set-shifting as a predictor of outcome in individuals with BN only in order to understand how this measure contributes to differential treatment response across diagnoses. Research into set-shifting in adolescents with BN would also be extremely informative, as to the author's knowledge, there has been only one study investigating the set-shifting abilities (including the TMT) of adolescents with BN (Darcy, Fitzpatrick, et al., 2012). That study found no set-shifting deficits compared to healthy controls.

It is possible that the measure of set-shifting employed in this thesis to test cognitive rigidity was insufficient on its own to fully capture the construct. Indeed, studies that specifically investigate set-shifting frequently employ numerous measures simultaneously, presumably to ensure that all possible facets of the construct are captured (Roberts et al., 2007). Future research investigating the contribution of set-shifting to outcome may similarly need to include a range of measures in order to fully determine if predictive effects exist. Given that cognitive rigidity is linked with perfectionism as a maintaining factor in at least one of the theoretical models (Schmidt & Treasure, 2006), the present results suggest it is specific perfectionism constructs, particularly the self-critical aspects, which influence outcomes, rather than set shifting. It is possible that perfectionism is simply more predictive of treatment outcome, including in terms of its interactions with other key theoretical variables. This is consistent with the position of the other two theories (Bardone-Cone et al., 2006; Fairburn et al., 2003), which specify perfectionism rather than cognitive rigidity.

6.3.5 Driven exercise.

The present results suggest that driven exercise as a compensatory behaviour may also be important in predicting outcomes, particularly in adolescent patients. In the adolescent sample, driven exercise at baseline was associated with worse eating pathology and quality of life at all time points, and also predicted lower weight over time. This contribution of driven exercise to treatment outcome has been surprisingly understudied in the eating disorder literature, particularly in individuals with BN, but several studies of AN have reported similarly negative outcomes associated with driven exercise in adults (Dalle Grave et al., 2012) and adolescents (Stiles-Shields et al., 2015). Some researchers have also reported high levels of exercise in individuals with AN not only in the acute phase, but also prior to illness onset and during childhood, leading to the suggestion that driven exercise might play an etiological role in the development and maintenance of eating disorders (Davis et al., 1997), and that driven exercise might represent a distinct subtype of AN (Davis & Kaptein, 2006).

Interventions specifically designed to reduce driven exercise in individuals with an eating disorder might be particularly helpful in improving outcomes, although few have been described. A randomized controlled trial of a program targeting compulsive exercise in eating disorders is currently underway, based on a model and an intervention developed at the University of Loughborough (Meyer, Taranis, Goodwin, & Haycraft, 2011). Interestingly the model contains perfectionism and rigidity, suggesting that these variables may share variance with compulsive exercise. There is some evidence that the addition of modified or 'safe' exercise programs can actually enhance outcomes in individuals with AN (Moola, Gairdner, & Amara, 2013; Zunker, Mitchell, & Wonderlich, 2011), and in inpatients with transdiagnostic eating disorder diagnoses (Calogero & Pedrotty, 2004). Encouraging patients to switch from driven exercise to such a program might be a useful avenue. It should also be noted that it is possible that our results around driven exercise were an underestimate of the actual effect,

because it was assessed via the self-report question from the EDE-Q which reads “Over the past 28 days, how many times have you exercised in a ‘driven’ or ‘compulsive’ way as a means of controlling your weight, shape or amount of fat, or to burn off calories?”. It is possible that many individuals with driven exercise might deny the frequency, or may in fact not endorse their exercise as ‘driven’, seeing it instead as a healthful behaviour. While there is no standard definition of driven exercise in the eating disorder literature (Mond, Hay, Rodgers, & Owen, 2006), interview-based approaches may more effectively elucidate the actual frequency of such activity.

6.3.6 Identifying predictors of drop-out and readmission.

It was surprising that no predictors of drop-out or readmission emerged in the adult sample. It is hard to know whether this is consistent with results from other research, as the majority of inpatient drop-out studies have considered AN only (Fassino et al., 2009), and few studies have examined readmission as a unique outcome measure. One explanation for the absence of predictors for these two outcomes is that some process that occurs post-admission is in fact responsible for the decision to drop-out, rather than baseline factors, while readmission might be better explained by processes that occur between discharge and follow-up. Unfortunately, the identification of such processes in clinical settings is challenging from a practical point of view, as frequent patient assessments between admission and discharge, and then again between discharge and follow-up, would be required to identify any such changes. This magnitude of patient burden was not feasible within the constraints of the clinical setting of the present research, but may be a valuable line of enquiry in more controlled treatment trials, where patients are aware of such requirements at the outset of treatment. Another possible explanation is that the sample was too small to detect such effects. In the case of drop-out, reviews have reported rates of 20-51 % for studies including both AN and BN (Fassino et al., 2009) and up to 57 % for AN only (Wallier et al., 2009). While our drop-out

rate of 22.8% in the adult sample is consistent with these figures, it is on the lower side, and our sample may therefore have been underpowered to detect an effect after it was split based on drop-out status.

6.4 Methodological Considerations

6.4.1 Disparate opinions about appropriate methodology.

The original conceptualization of moderation and mediation was described by Baron and Kenny in 1986 (Baron & Kenny, 1986), and continues to be used today. However, these concepts have since been updated with respect to treatment outcome (Kraemer et al., 2008; Kraemer et al., 2001; Kraemer et al., 2002). These guidelines suggest that a variable (M) is a moderator of the relationship between another variable (T) and an outcome (O) if M precedes T and if M and T are not related. In the case of mediation, a variable (M) can be said to mediate the effect of another variable (T) on outcome (O), if T precedes M, and that the relationship between T and O is different when M is not included in the analyses compared to when it is. Non-specific predictors are defined as baseline variables that have a main effect on outcome. It should be noted that the definitions of moderation and mediation in outcome research were developed for use within, and have primarily been applied to, randomized controlled trials (RCTs). In this context, researchers are interested in knowing whether moderators or mediators exist in the context of different types or levels of treatment, and treatment type is always included in the analyses as one of the potential predictor variables.

Unfortunately, few guidelines are given about how to define more complex processes in the naturalistic settings like those examined in this thesis, where treatment type did not vary across individuals. This lack of specific guidelines was reflected in the review process of the studies in this thesis. As described in Chapter 1, each study in this thesis underwent comprehensive peer review prior to inclusion as a chapter, revealing a diversity of opinions about how the questions of prediction should best be conceptualized and analysed. Notably, the reviewers of the adult and adolescent manuscripts had different opinions about the analytic approach. Specifically, there was a lack of consensus about how to best define and statistically test the concepts of simple prediction, moderation and mediation.

Problems also arise when other types of more complex predictive processes that do not meet the strict guidelines are considered. According to Kraemer et al (2002), any type of predictor that does not fit the strict guidelines given for identifying moderators and mediators in RCTs should be considered a non-specific predictor. However, there are a number of predictive processes that provide important and complex insights over and above these more simple cases. For example, baseline variables may interact to predict outcome, and several recent studies have reported such results. The combination of low self-compassion and high fear of self-compassion predicted poorer treatment response in transdiagnostic inpatients (Kelly et al., 2013), while different combinations of baseline weight suppression and baseline BMI interacted to predict outcome in adults with AN in residential treatment (Berner et al., 2013). Finally, poorer social adjustment at baseline combined with a lower BMI predicted a poorer response to outpatient cognitive behaviour therapy for adults with BN (Agras et al., 2000). In each of these cases, as there is only one type of treatment, and it is difficult to establish which of the two predictor variables had temporal precedence, it is difficult to establish the necessary criteria for strictly defined moderation. There do not appear to be any guidelines about how to define this kind of predictive process, other than those already described which would label the process as non-specific prediction.

Another example of an interaction that is not covered by the strict definitions is apparent in the adolescent sample in this thesis, where interactions were examined between a baseline variable and time. In this case, time was acting as a categorical variable with three levels (baseline, discharge and follow-up). This kind of interaction has been reported (Kelly et al., 2013), but like the interactive baseline examples given above, does not meet the strict definition of moderation. Such analyses are however distinct from, and provide insight over and above simple baseline predictors. For example, in the case of variable by time interactions, these analyses explain at what different ‘level’ of time a predictor exerts its

effects, just as one might be interested in finding out at what different 'level' of treatment a predictive effect might occur.

Another such example shown in the present research (and in numerous previous studies as described in Chapter 2, involves change in a putative predictor variable during treatment predicting outcome. This clearly describes a process that is different to a standard non-specific, baseline predictor of outcome, but according to strict guidelines should be labelled as a non-specific predictor (Kraemer et al., 2002). This lack of distinction is potentially problematic, as the two different scenarios have quite different clinical and research implications. The first (non-specific predictor) provides valuable prognostic information, and even tells us something about how we might need to tailor treatment choices to better suit individuals with one or other baseline characteristic (e.g., if males are found to do particularly well in a treatment, while females make almost no progress, it might be preferable to offer females some other kind of intervention). Conversely, the second type of prediction tells us about what changes we need to be striving towards during treatment in order to ensure patient gains. As in the present research, if improvements in eating pathology during treatment are strongly predictive of outcomes at follow-up, it follows that every effort should be made to ensure that therapeutic intervention encourages robust symptom change.

At least in the case of change in a predictor variable during treatment, one approach that potentially solves the lack of distinction has recently been described (Kuyken et al., 2010). This requires specifying whether change in a variable during treatment is a main effects mediator (i.e., where change in a predictor variable during treatment impacts outcome irrespective of treatment type) or an interactive mediator (i.e., where change in a predictor variable during treatment impacts outcome differentially across treatment types). This approach provides a useful distinction. It might be that a similar approach could be applied to the moderational scenario described above, where the interaction between two baseline

variables where temporal precedence is not clear and only one type of treatment exists could be said to be non-specific moderation, as opposed to moderation that occurs in the more traditionally described contexts.

In order to ensure that clear, clinically applicable results are obtained across studies in the future, it will be important to continue to define the various complex analyses that go over and above simple, non-specific baseline prediction, but do not meet the strict definitions of moderation or mediation. While several suggestions have been provided here, it is also likely that simply including complex analyses in future studies will go some way to improving the current state of affairs. This will help to generate the necessary consideration and debate about how different types of processes should be measured, analysed and reported, which to date has been limited by the relatively small number of complex analyses being reported.

6.4.2 Prediction versus causation.

It is important to note that the goal of the present research was to identify predictors of outcome, rather than causal factors. While some of the predictors identified may well have a causal effect on outcome, the present analyses do not allow for these kinds of conclusions to be drawn, as it was not within the scope of the research to control for the myriad of potential confounding factors that may also have contributed to outcomes. Instead, the present research has identified factors that deserve further investigation in future research that develops and implements interventions that manipulate the identified predictors.

6.4.3 Selection of theoretical variables.

The theoretical predictor variables tested in the two empirical studies in this thesis were selected based on their appearance in three prominent models of eating disorders. This approach was chosen to ensure that the selected variables would be most likely to have robust application across age groups and in the transdiagnostic setting. The models also included potential predictors that were not shared. However, the clinical setting in which the present

research was conducted required that patient-burden be carefully considered, and did not therefore permit the examination of variables that were not shared across the models, nor a thorough testing of each model. Accordingly, the theoretical conclusions drawn from the present results can only be considered to support the shared components of the models. Notably, one potential predictor that was not able to be examined in the present research was interpersonal functioning and relationships with carers. These factors are particularly prominent in the Cognitive Interpersonal Model (Schmidt & Treasure, 2006; Treasure & Schmidt, 2013), and were recently shown to predict eating disorder symptoms in adults receiving intensive inpatient or day hospital treatment (Goddard et al., 2013). It would be valuable for future studies to incorporate measures of interpersonal functioning as potential predictors of outcome in conjunction with the variables identified in the present research (i.e., perfectionism, mood intolerance and ineffectiveness).

6.4.4 Statistical power.

The sample size in both the adolescent and adult studies should be noted as a potential limitation. In addition, the adolescent sample was significantly smaller than the adult sample due to the constraints around data collection in the paediatric setting. Given the limitations around sample sizes, our analyses may have been underpowered to identify some effects. Repeating the present analyses with larger samples will be an important goal for future research in order to obtain a more robust understanding of outcome in this patient group.

6.4.5 Length of follow-up.

The follow-up period was only three months, given the time constraints associated with the thesis framework, and as such conclusions about predictors of outcome during the follow-up period cannot be extended to the longer term. Repeating the assessments at longer follow-up intervals will be an important direction for future research in order to understand whether the same predictive processes are associated with longer term change.

Related to the follow-up length, the shorter time frame meant that very few individuals could be classified as 'recovered', and so it was not possible to examine predictors of recovery. The most robust and recently recommended definition for recovery for eating disorders (Bardone-Cone et al., 2010) which can be applied transdiagnostically, includes a combination of: (i) no longer meeting criteria for an eating disorder, (ii) abstinence from bingeing, purging and fasting for 3 months, (iii) body mass index ≥ 18.5, and (iv) eating pathology scores (e.g., as measured by the EDE-Q) within 1 SD of healthy, age-matched population norms. Virtually none of the participants in the current datasets met this definition of recovery by the three month follow-up, thereby excluding the possibility of comparisons between recovered and non-recovered groups. For this reason, improvement in these key variables, with the addition of drop-out and readmission, were instead considered as outcome variables in this thesis. However, it would be useful to understand if the same processes are ultimately associated with recovery. Patient follow-up at longer intervals following treatment would assist with bolstering the numbers of recovered individuals to allow such analyses.

6.4.6 Treatment engagement post-discharge.

Unfortunately, data about patients' engagement in ongoing outpatient treatment or other support services between discharge and follow-up was not available for the two samples collected for this thesis. While relatively little is known about the extent to which such engagement is related to longer term outcomes, there is some evidence that it might play an important role in maintaining treatment gains. One study of adults who received outpatient treatment for BN found that those who used more social support strategies in the month following treatment completion did significantly better at six-month follow-up (Binford et al., 2005). In terms of post-discharge treatment engagement, it is not known whether engaging in treatment following an inpatient stay, and if so, which kind of treatment, might be most important in facilitating ongoing change. A detailed investigation of this question in similar

samples would be a valuable direction for future research, as it would help greatly with discharge planning and the selection of ongoing support mechanisms.

6.4.7 Findings limited to inpatient setting.

As all empirical data used in this thesis was collected in inpatient settings, the conclusions drawn cannot be extended to outpatient eating disorder treatment. This is a particularly important consideration when interpreting the findings from the adolescent sample, as the inpatient treatment they received included a primary focus on medical stabilization and weight restoration, which is distinct from more cognitive or family-based approaches typical of outpatient modalities (Hay et al., 2014; Sylvester & Forman, 2008). Ongoing research across all treatment settings will be essential in order to understand the factors associated with outcome differentially across modalities, and how treatment type might moderate outcome. Also in relation to treatment setting, neither of the inpatient units where the present data was collected admitted patients with a diagnosis of BED, so no BED cases were available for the present analyses and therefore results relate only to AN, BN and OSFED cases.

6.4.8 Small numbers of male patients.

An important limitation across both the adolescent and adult studies was the small numbers of males included in the samples. The decision to exclude or include such cases is challenging, as it is unclear whether differences exist between the two groups that would impact on the validity, and ultimately the clinical applicability, of results. Research has highlighted some differences in the clinical characteristics, particularly a tendency for lower self-reported weight and shape concerns in males (Raevuori, Keski-Rahkonen, & Hoek, 2014; Shu et al., 2015). Conversely, many clinical characteristics across the sexes are shared, both in adolescents (Welch et al., 2015) and adults (Woodside et al., 2001). Further, and perhaps of particular relevance to the present research, men and women appear to respond to intensive

treatment in a similar manner (Woodside & Kaplan, 1994). On balance, and after careful consideration, it was decided to retain the male cases for inclusion in the present research.

It was also considered important to include these cases in the present research because it is unlikely that sufficient numbers will be available for an exclusively male study in any near future. The small numbers available in the present research appear to be consistent with the situation at large. One study that sought to describe the aetiology, clinical characteristics and prognosis of male eating disorder patients over a 14 year period (using a retrospective design), was able to include only 135 cases in the final analyses (Carlat, Camargo, & Herzog, 1997), despite including all cases that presented to both a large hospital and its outpatient clinics. In another study that considered consecutive referrals to a specialist adolescent eating disorder service, only 53 young males (versus 704 females) were referred in a 17-year period (Shu et al., 2015). This under-representation of males in eating disorder treatment settings is no doubt responsible for their under-representation in the existing literature base.

Clearly, studies examining exclusively male samples that can be undertaken in a feasible and time-efficient way are much needed. To the author's knowledge, no studies to date have examined predictors of treatment outcome in an exclusively male sample, nor compared predictors of outcome between men and women with eating disorders. To this end, collaboration between treatment centres in order to obtain sufficient numbers is strongly recommended as a strategy.

6.4.9 Real-world nature of the treatment setting.

A note on the nature of the research setting in which these two studies were conducted is also warranted, as this represents both a strength and a limitation of this thesis. In order to gain access to an adequate number of patients to properly investigate the primary research questions, it was necessary to conduct this research at a large, public and teaching tertiary hospital in South Australia. At the time this was the only facility in the region with ongoing,

specialist treatment programs for both adult and adolescent eating disorders. Accordingly, the units operate as 'real-world' treatment centres with routine clinical demands**.** Conducting research in this kind of setting comes with inherent challenges, but also enables the gathering of insights that have real-world applications. One challenge is that modifications to the treatment protocols are implemented periodically to ensure up-to-date evidence-based approaches are applied, to respond to changing service demands, and to accommodate budgetary challenges. This is entirely consistent with the notion that complex treatment interventions should where possible be tailored to local settings, rather than rigidly standardized (Craig et al., 2008), but means that treatment is not delivered under the tightly controlled parameters typical of treatment trials. The potential confounding effect of this should be considered when interpreting the current results.

Second, because of the busy clinical nature of the treatment units, it was necessary to consider patient-burden when developing the assessment procedure. This meant that limits had to be placed on the number and nature of measures administered, and on the number of times the assessment could be completed. As already discussed, a full examination of the theoretical models was not possible under these constraints. There are, however, several considerable benefits of this kind research. First, given that the present results were obtained from a busy clinical setting, they can be considered to be broadly applicable to similar real-world settings, a conclusion that cannot always be drawn when trying to extrapolate results from tightly controlled trials. Second, this kind of research helps to contribute to ongoing clinical improvement processes in real-world clinical settings. Specifically, it is essential to ensure that clinical practice is routinely evaluated, reported on, and ultimately that evidence-based changes are implemented (Craig et al., 2008). The results reported in this thesis have already informed the implementation of clinical improvements on the two units in question, contributing to this important ongoing process.

6.5 Conclusion

This thesis has advanced the current understanding of predicting outcomes in individuals receiving treatment for an eating disorder. By adopting a rigorous, theoretically informed approach to this question, the present research identified a range of predictors, moderators and mediators of outcome. A strong clinical focus on weight gain for adolescents in the inpatient setting, and on improvement in psychological variables for transdiagnostic adult inpatients, appear to be important in driving therapeutic change that persists post-discharge, and future research should continue to explore these associations. While the theoretical predictors need to be tested in more controlled settings to better understand their effects, perfectionism appears to be particularly important as a potential target for interventions that might improve clinical outcomes.

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