

Pre-Treatment Patient Characteristics as Predictors of Drop-Out and Treatment Outcome in
Individual and Family Therapy for Adolescents and Adults with Anorexia Nervosa:
A Systematic Review and Meta-Analysis

Eva. C. Gregertsen^a, William Mandy^a, Natalie Kanakam^b, Stephanie Armstrong^b, Lucy Serpell^{ab}

^{1a}Department of Clinical, Educational, and Health Psychology, University College London,
London, UK

^{2b}North East London Foundation Trust, London, UK

Corresponding author:

Eva C. Gregertsen

eva.gregertsen.15@ucl.ac.uk

1-19 Torrington Place

London, UK

WC1E 7HB

1. Introduction

Anorexia nervosa (AN) is a debilitating eating disorder associated with a range of psychosocial impairments and, in severe cases, mortality (Zipfel et al., 2015). The disorder is notoriously difficult to treat, with between 31-50% of inpatients, and 23-57% of outpatients, dropping out prematurely (Carter et al., 2006; Carter, et al, 2004; Carter et al., 2012; Halmi, 2005; Schnicker et al., 2013), and only half of all patients receiving treatment achieving full recovery (Steinhausen, 2002). As such, identification of predictors of outcome and drop-out is essential in the quest for improving AN treatment, as pinpointing variables related to prognosis might facilitate more specialised interventions for those who are identified at an early stage as at risk for a poor outcome. Furthermore, identification of prognostic factors can lend important insight into the mechanisms of AN, which can help inform and improve upon current interventions.

Despite recent trends to attempt to identify commonalities across eating disorders diagnoses in order to inform trans-diagnostic treatment approaches (Dalle et al., 2013; Fairburn et al., 2003; Wade et al., 2006), some researchers suggest there are likely to be distinct predictors in AN, compared to other eating disorders (Birmingham et al., 2009), which calls for the need to carry out a focused, AN-specific review. A recent review and meta-analysis conducted by Val and Wade (2015), whilst comprehensive in scope, rendered a gap in the literature in that predictors were assessed in terms of their relation to AN, bulimia nervosa (BN), and binge eating disorder (BED) as an aggregate, as opposed to individually. The problematic nature of this resides in the fact that AN differs from BN and BED both in terms of symptomatology, aetiological factors, and criteria for good outcome. With regards to outcome, the issue of weight particularly demonstrates why assessing eating disorders as an aggregate is troublesome, as weight gain is a critical aspect of good outcome for AN yet may demonstrate poor outcome or be neutral for other eating disorders. Further highlighting issues arising from assessing eating disorders as an

aggregate, Val and Wade (2015) hypothesised that lower levels of depression would be associated with a more positive prognosis in eating disorders; however, upon further scrutiny, this statement was revealed only to be applicable for BN patients, with studies examining AN patients finding no association between depression and success within treatment (Le Grange et al., 2014; Speranza et al., 2007). Considering these issues, predictors may be best understood if the disorder is considered on an individual basis, as predictive variables pertaining to eating disorders may not necessarily apply trans-diagnostically. However, whilst reviewing AN on an individual basis as opposed to trans-diagnostically allows for a better understanding of predictors, one issue which still remains is the disparate definitions of both outcome and drop-out within the literature, with few studies demonstrating a consensus as to how these outcomes are defined, thereby rendering comparison problematic.

Considering the most recent reviews pertaining to AN specifically, one review of 35 studies examined sociodemographic predictors of treatment, finding only weak evidence to support the predictive value of variables associated with outcome (Bulik et al., 2007). A second review of seven studies, attempting to identify predictors of drop-out, concluded that evidence in support of the presence of robust predictors of drop-out from AN treatment was both conflicting and scarce (Wallier et al., 2009). The only factor shown to consistently predict drop-out was greater binge/purge behaviours. Clearly, an updated review integrating the past decade of research would be useful to elucidate more clearly the predictive value of baseline variables on outcome and drop-out in AN treatment.

1.1. Aims

While multiple studies have investigated potential predictors of drop-out and outcome in treatment of AN, development of a cohesive and up-to-date picture of the research literature has yet to be achieved. As such, the current review and meta-analysis aims to systematically

investigate the existing AN literature and present a comprehensive summary of the evidence for predictors of drop-out and treatment outcome in patients with AN, as well as to highlight the strengths and limitations within the current literature.

2. Methods

2.1. Information Source and Search Strategy

The current study was conducted and reported in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Moher et al., 2009). The primary search strategy utilised multi-field searches within four databases, PsychInfo, Medline, Embase, and PubMed. All four databases were searched from the beginning of the databases to March 2018 using the following terms: (anorexia) and (treatment OR therapy OR psychotherapy) and (response OR outcome OR drop-out OR attrition OR premature termination OR treatment acceptance) and (predictor OR predict). Hand searches of bibliographies of identified studies and relevant reviews were conducted to identify any additional pertinent studies not identified in the electronic search.

2.2. Inclusion/Exclusion Criteria

Empirical studies that (a) were published in English in a peer reviewed journal, examining (b) pre-treatment patient variables as predictors of outcome and/or drop-out in (c) treatment with (d) a formal diagnosis of AN restrictive or binge-purge subtype, or atypical AN, in cases wherein BMI was <19, according to DSM-III, -IV, or -V (Diagnostic and Statistical Manual of Mental Disorders) or ICD-9 or -10 (International Statistical Classification of Diseases and Related Health Problems International Classification) criteria were included. Studies reporting results from individuals without a formal diagnosis of AN according to DSM or ICD criteria were excluded. Of note, broadly defined AN (defined as either atypical anorexia or Eating

Disorder Not Otherwise Specified depending on which year the relevant study was conducted and which diagnostic manual was utilised) included individuals whose disorders fulfilled some of the features of AN but in which the overall clinical picture did not justify the diagnosis, for example in instances wherein all the criteria of AN were met except the weight criterion (American Psychiatric Association, 2013; Thomas et al., 2009; World Health Organisation, 1992).

2.3. Study selection

Search outputs from the three databases were first cross-referenced for duplicates which were removed before examining the results. Then, abstracts were assessed by the first author against inclusion criteria as well as to determine whether they broadly pertained to the review questions. The full-text of all remaining studies was then reviewed to determine eligibility for inclusion in the meta-analysis, including effect size calculation. If studies did not present sufficient data to calculate an effect size, the authors of the relevant study were contacted in order to attempt to attain the necessary data to calculate effect sizes. To check its reliability, a second blinded rater (N.K.) was provided with a random sample of 100 of the 988 articles identified in the primary search and evaluated these against the criteria for inclusion. A third blinded rater (A.S.) examined an additional 147 articles. There was perfect (i.e. 100%) agreement achieved upon comparing the initial and the second and third (blinded) rater decisions regarding which articles met criteria for inclusion in the review. Presented in Fig 1 is a flow diagram of the selection process guided by the PRISMA guidelines.

2.4. Quality Assessment of Included Studies

The methodological quality of included studies was assessed in accordance with the STROBE statement (see Table 1). The STROBE checklist comprises 22 items assessing the

quality of scientific articles. The checklist was utilised to calculate the percentage of STROBE criteria met by each paper, known as the STROBE score. Presented in Table 1 are these scores in descending order. Overall quality assessment from A-C was used in place of a sum score (Jüni, Altman and Egger, 2001). Previous reviews have utilised this method (Olmos, Antelo, Vazquez, Smecuol, Maunno, & Bai, 2008; Teti, Rebok, Rojas, Grendas, & Daray, 2014). The three categories of global quality assessment include: A) the study met more than 80% of STROBE criteria, (B) the study met between 50–80% of STROBE criteria, or (C) the study fulfilled less than 50% of STROBE criteria.

2.5. Data Extraction

For each category of predictor of drop-out and outcome, data was extracted from all studies featuring that predictor. This included the study type (ie. prospective or randomised control trial), the number of participants included in the analysis for that specific predictor, treatment method, definition of the outcome variable, and the predictor measure. Characteristics of the studies included in the meta-analyses are presented in Table 2.

2.6. Grouping Effects

In some instances, multiple effect sizes for one predictor of outcome were calculated from the same study, as the result of a single predictor having been used to predict more than one type of outcome (e.g. eating disorder pathology and BMI). As it is not recommended to include multiple effects from a single study when conducting meta-analyses, as this would increase the likelihood of a single study having undue influence on results, effects of a predictor were combined into an aggregate effect size in instances where multiple types of outcome were presented for a single predictor. Presented in Table 3 are the final outcome groupings utilized in the analyses.

Furthermore, due to the disparity of definitions of drop-out and outcome within the literature, we opted not to include a definition of drop-out and outcome to ensure the review be as inclusive as possible. Thus, specific outcome/drop-out definitions per study are presented in Table 2.

2.7. Statistical analysis

2.7.1. Effect sizes

Due to correlation coefficients having been shown to best enable interpretation of the practical significance of an effect (Field, 2001), as well as having been previously utilised in similar meta-analyses of predictors of outcome in eating disorders (Vall and Wade, 2015), an effect size expressed as the correlation coefficient, r , was calculated for each predictor variable for drop-out and outcome by entering the reported or obtained statistical outcomes into an effect size calculator. For a study to be included in the analysis, sufficient statistics for an effect size to be calculated had to be provided. Effect sizes were calculated for both significant and non-significant findings alike.

2.7.2. Publication Biases

To determine the effect of the “file-drawer problem”, referring to the tendency of positive results to be published over negative or non-confirmatory results, the “fail safe N” was calculated for each meta-analysis, wherein the “fail safe N” denotes the number of additional ‘negative’ studies (studies in which the effect was zero) that would be needed to increase the P-value for the meta-analysis above 0.05 (Rosenthal, 1979). In instances wherein this estimate is larger than the number of studies included in the meta-analysis, there is a greater likelihood that the calculated meta-analytic effect is robust to this type of publication bias.

2.6.4. Method of meta-analysis

Only predictor variables featured in at least three studies were included in the meta-analysis. A random effects model, which assumes that data being analysed are drawn from a hierarchy of different populations, was utilised, thus allowing inferences to generalise beyond just those studies included in analysis. As per the Hedges and Vevea method of meta-analysis (Hall and Brannick, 2002), effect size were first transformed into a standard z metric before scores were averaged. Importantly, each effect is weighted based on study sample size with this method. Heterogeneity was measured by the Q statistic, which is computed by summing the squared deviations of each study’s effect estimate from the overall effect estimate, with each study’s contribution weighted by its inverse variance. (Cochran, 1954). Inverse variance weights each variable in proportion to its variance, meaning that larger studies, which yield smaller standard errors, will have more ‘weight’ than smaller studies.

3. RESULTS

3.1. Predictors of Drop-Out and/or Outcome

Criteria for inclusion for the meta-analysis was met by 27 studies, wherein included studies assessed at least one predictor variable for which there were sufficient data presented or obtained to calculate an effect size, and the predictor was featured in at least two other studies. Given in Table 2 are the characteristics of the studies included in the meta-analysis. Presented in Table 3 are the results of the meta-analysis, wherein predictor variable's relationships with drop-out and negative outcome are presented.

3.1.1. Drop-out

Displayed in Figures 2, 3, and 4 are the forest plots for the three significant predictors of drop-out. Motivation demonstrated a small but significant negative relationship with drop-out ($r = -0.21$, 95% CI [-0.38, 0.01], $p = .042$), wherein drop-outs demonstrated lower levels of motivation at baseline than those who completed treatment. The associated Nfs was adequate (i.e., $Nfs > Nstudies$). Notably, studies were just as robust in detecting findings whether motivation was measured by 6 motivational questions or the more sophisticated and comprehensive ANSOCQ. Furthermore, there was a significant, small effect of AN subtype on drop-out ($r = 0.12$, 95% CI [0.04, 0.19], $p < .005$), wherein AN patients with the binge/purge subtype were more likely to leave treatment prematurely than their restricting counterparts. Additionally, admission BMI demonstrated a small, negative relationship with drop-out ($r = -0.12$, CI [-0.18, 0.06], $p < .005$). The associated Nfs added confidence to these two findings.

The remaining predictors demonstrated negligible to non-existent associations: ED pathology ($r = -0.09$, CI [-0.02, 0.20], $p > .05$), age ($r = 0.03$, CI [-0.08, 0.14], $p > .05$), general psychopathology ($r = -0.07$, CI [-0.25, 0.10], $p > .05$), depressive symptoms ($r = -0.05$, CI [-0.15,

0.06], $p > .05$), previous hospitalisations ($r = 0.03$, CI [-0.09, 0.15], $p > .05$), age at onset ($r = -0.01$, CI [-0.01, 0.07], $p > .05$), and Axis I or II comorbidity ($r = 0.03$, CI [-0.20, 0.26], $p > .05$).

3.1.2. Outcome

Displayed in Figures 5 and 6 are the forest plots for the two significant predictors of outcome. Motivation demonstrated a small but significant negative relationship with outcome ($r = -0.27$, 95% CI [-0.44, -0.08], $p = .006$), with patients demonstrating higher motivation for recovery at baseline showing greater outcomes, with the estimated Nfs adding confidence to the finding. Moreover, severity of ED pathology was shown to have a significant small, positive relationship with outcome ($r = 0.23$, 95% CI [0.04, 0.47], $p = .023$), wherein AN patients with greater ED symptoms at baseline showed poorer outcomes at discharge, with the estimated Nfs adding support to this result. Further, B/P subtype demonstrated a small positive association trending towards significance ($r = 0.13$, 95% CI [-0.01, 0.33], $p = .057$), wherein those who suffered from the B/P subtype of AN tended to show poorer outcomes than their restricting counterparts.

The remaining predictors demonstrated small to negligible associations: general psychopathology ($r = 0.32$, CI [-0.06, 0.62], $p > .05$), illness duration ($r = 0.15$, CI [-0.03, 0.26], $p > .05$), admission BMI ($r = -0.07$, CI [-0.29, 0.16], $p > .05$), age ($r = 0.09$, CI [-0.07, 0.25], $p > .05$), and depressive symptoms ($r = 0.07$, CI [-0.10, 0.23], $p > .05$).

4. DISCUSSION

The aim of this systematic review and meta-analysis was to identify and quantify the predictive value of factors associated with drop-out and outcome for patients receiving therapy for AN. Consistent with conclusions from other reviews that our current understanding of AN

predictors is limited as findings are sparse and inconsistent, few pre-treatment patient variables were found to predict drop-out or outcome on a reliable basis, and the divergent variables and methods between studies make drawing definite conclusions a difficulty (Bulik et al., 2007; Vall and Wade, 2015; Wallier et al., 2009). Nevertheless, there's some evidence for the predictive validity of the following pre-treatment variables, shown to predict higher risk of drop-out within the current meta-analysis: 1) lower motivation; 2) having the binge/purge subtype of AN; and 3) having a lower BMI at admission. Furthermore, regarding outcome, the following variables measured prior to treatment showed significant associations with poorer response to therapy: 1) greater ED pathology and 2) poorer motivation.

4.1. Clinical implications

There are several clinical implications to be considered regarding the aforementioned findings. Firstly, considering the predictive validity of baseline motivation on drop-out and outcome, increasing motivation may be an important strategy to facilitate the likelihood of patients remaining in treatment, as well as engaging with treatment whilst in attendance (Vitousek et al. 1998; Ward et al., 1996). Whilst the results of attempts to increase motivation through motivational interviewing have showed mixed success rates (Dray and Wade, 2012; Knowles et al., 2013; Macdonald et al., 2012), it may be that patients who stay within treatment are generally those who are already relatively motivated to recover, and that those patients who would have benefited most from techniques aimed to enhance motivation simply do not remain in treatment for a long enough duration for motivation enhancement strategies to take an effect. As such, and considering that drop-outs can be differentiated from treatment completers in terms of motivation at baseline, it seems essential to consider a patient's motivation for recovery at assessment stages, so that patients who are determined to be at risk for drop-out or poor outcome due to low motivation for recovery are quickly identified, allowing therapy to be

tailored to include a component aimed at assessing and increasing motivation at an early stage in treatment.

Secondly, having the binge-purge subtype of AN was also linked with drop-out. Individuals with the binge-purge subtype of AN have been shown to demonstrate higher levels of impulsivity than their restrictive counterparts (Klump et al., 2000), which could help explain why these individuals are more likely to terminate treatment prematurely. Our finding suggests that clinicians and care team staff should take particular care to consider AN subtype in terms of treatment conditions and take particular effort to engage and retain AN-BP patients in care as they are more likely to drop out than their AN-R counterparts. This similarly applies to patients demonstrating a lower BMI. Patients with a lower BMI may be more likely to drop out from treatment for numerous reasons. For instance, lower BMI can be considered an indicator of illness severity; thus, the more severely underweight the patient is, the more psychologically ingrained their illness may be. In such cases, the patient may either fail to desire recovery due to deeply identifying with their disorder, or may not consider recovery an achievable option due to the degree to which they feel their illness is in control of them, both circumstances leading to increased likelihood for drop out. Of importance, more severely underweight patients are at highest medical risk if they do not receive effective treatment; thus, it is especially important that efforts are made to prevent these patients from dropping out.

Moreover, considering that eating disorder pathology measured at baseline predicted how well patients fared in treatment, it seems important to identify AN patients with more severe ED psychopathology at assessment, as these patients are less likely to have successful outcomes from therapy. Having such assessments in place may increase treatment success for these at-risk patients in that clinicians may decide to implement more intensive or frequent treatment for patients displaying more extreme ED pathology.

Furthermore, based on qualitative research into reasons for drop-out in AN treatment, suggestions have been posted within the literature for how premature disengagement may be prevented (Eivors et al., 2003). Firstly, Eivors et al. (2003) posed that, particularly in the early stages of treatment, clinicians should seek a shared understanding of the meaning of the illness with the patient, viewing it as a ‘coping mechanism’, albeit a faulty one, rather than a means of self-destruction. Such a focus may increase a feeling of collaboration between therapist and patient, which may help motivate the patient to carry on with treatment. Secondly, the authors suggested that it may be of benefit to have one therapist focusing on longer-term psychotherapeutic aims, whilst food intake and weight is monitored by another member of the care team. The rationale behind this suggestion is that if one of the objectives of therapy is to develop a sense of self distinct from that defined by eating behaviour, whilst also encouraging weight gain, a dual role for the therapist wherein both these facets are monitored by the same individual may not be conducive to this process.

4.2. Limitations of current research

There are still considerable gaps and inconsistencies in the AN literature which limit the extent to which definite conclusions can be drawn. Thus, it seems necessary that a higher degree of replication and consistency among findings are achieved before empirical results can warrant changes to clinical practice and treatment approaches.

Firstly, across the studies assessed herein, outcome measures varied considerably, with some studies utilising BMI gains as a measure of outcome, others utilising a certain BMI threshold which needed to be reached to be considered recovered, and others still utilising aggregate scores of BMI and ED pathology measures, or ED pathology measures alone without considering BMI. Needless to say, such disparate definitions of treatment outcomes are problematic, as they render comparison across studies a very difficult task. Despite the clear

necessity for agreement amongst researchers and clinicians (and patients) on what defines recovery, there is no current “global consensus” on this definition, thus perpetuating the status quo wherein outcome measures vary widely within the AN literature (Bachner-Melma et al., 2006; Jarman and Walsh, 1999; Kordy et al., 2002). One solution to this problem would be to compare studies according to outcome measures utilised; however, the current dearth of studies examining predictors in AN renders this problematic for meta-analysis.

Similarly, drop-out has also been poorly defined in the AN literature. To exemplify, one study within this review defined drop-out as “patients self-discharging against medical advice or simply leaving inpatient setting resulting in the designation of absent without leave” and specifying that inherent to the definition of drop-out was that treatment had ended as a result of the patient's unilateral decision (Surgenor et al., 2004), whereas other studies considered patients to have dropped out when they were discharged by the therapist as a result of not complying with treatment or reaching their target weight, with others still defining drop-out as attending less than a certain percentage of treatment sessions. Another issue which needs considering is that patients sometimes require hospital admission for medical stabilisation. In such instances, hospitalised patients may be recorded as drop-outs in certain studies, whereas other studies may allow brief hospitalisations as part of the outpatient treatment. Thus, it seems necessary, although challenging, that researchers adopt definitions of drop-out and outcome which are similar enough to allow valid cross-study comparison.. A review of attrition in outpatient treatment for AN made note of several flaws in reporting drop out, and put forth a suggested framework for how drop-out from eating disorder treatment might ideally be reported (Mahon, 2000). Specifically, Mahon (2000) emphasised the importance of agreeing on a multi-dimensional definition of drop-out wherein three important facets are considered. Firstly, the author distinguished between patients who leave regular treatment with a therapist, and patients who leave the treatment-phase of a controlled study, termed treatment-phase attrition, rather than

drop-out, in this framework. Secondly, the author emphasised how to qualify a patient as a drop-out, noting that having attended at least one therapy session is an important criterion (Garfield, 1994), and further suggesting that treating drop-out as a continuous variable and reporting on the number of therapy sessions attended relative to the amount of treatment expected in order for the patient to improve would allow for comparison of levels of dropping out (early versus late) and of treatment types. Lastly, it was noted that a final task would be deciding whose viewpoint to utilise in deciding whether the termination of therapy was in fact early, as patients and clinicians may disagree upon this point (for instance, a patient might leave therapy having genuinely received all the help she wanted, thereby considering herself a completer, wherein her therapist would have liked her to achieve more, thereby considering the patient a drop-out) (Mahon, 2000). Arguing that there is limited evidence as to the difference between types of dropping out regarding outcome, clinical differences, and predictor variables (Wallier, 2009), Sly (2009) suggested adopting an overarching definition of 'premature termination of treatment' (PTT) to include all patients who withdraw from treatment due to a unilateral decision made either by themselves or staff. Sly (2009) further proposed that drop-out should then be categorised according to two factors: who initiated the termination (patient-initiated versus staff-initiated), and the timing of the termination (early versus late). Expanding on the notion of describing drop-out sufficiently with an even more descriptive framework, DeJong, Broadbent et al. (2012) proposed a reporting structure for drop-out, including reporting reasons for dropping out, wherein reasons should be classified within the following categories: clinical (wherein patients are withdrawn for medical/therapeutic reasons, for example being hospitalised due to continued weight loss); logistical (wherein patients are withdrawn for practical/logistic reasons such as moving to another city); progress (wherein patients are withdrawn by mutual agreement between patient and clinician due to good therapeutic progress and based on predefined targets, e.g. BMI > 18.5 and symptom score within one standard deviation of the

population mean); and patient-initiated withdrawal (wherein the patient discontinues without agreement from the clinician).

Furthermore, treatment methods in the studies within this review varied considerably, with treatment forms including CBT, SSCM, psychodynamic therapy, diet counselling, and interpersonal psychotherapy, in various combinations, both within inpatient and outpatient treatment. In some studies, the treatment was poorly specified. One approach to this challenge could be narrowing the scope of the review by considering only one mode of therapy at a time when systematically reviewing predictors of drop-out and outcome in AN treatment. However, due to the paucity of studies found in this particular area, there would be unlikely to be enough studies for sufficient analysis. Thus, in order to overcome this issue and allow for cross-comparison, emphasis should be placed on adequate description of treatment methods utilised in each specific study. This way, the reader is ensured awareness of how treatment methods may have differed, and can consider how such variations across studies may hold relevance for results.

Another issue which warrants mentioning is the disparity across studies in how some baseline predictors were measured. For example, in terms of depression and anxiety, some studies measured depression/anxiety on a present/absent basis as determined by a clinical diagnosis of a depressive episode or anxiety disorder, whereas others measured depression/anxiety on a spectrum utilising scales such as the BDI, or the anxiety subscale of the BSI. In terms of motivation, the majority of studies captured the variable using the ANSCOQ, a psychometric scale based on the trans-theoretical model of change developed specifically for AN to capture readiness for change, whereas one study included only a single item in order to determine motivation. One approach to overcome issue in future research would be to provide clear and stringent measurement criteria to determine whether a predictor variable is eligible for inclusion (e.g. depression being defined as presence of a minor or major depressive episode, or motivation as determined by a psychometric scale such as the ANSCOQ or RMQ); however, due

to the withstanding paucity of studies in the literature, we opted for a more inclusive approach in the current review.

Another issue to consider is the range of severities and presentations within AN. As is true for any clinical disorder, no case presents exactly the same. This variation may produce difficulties in assessing treatment success. For instance, if recovery is defined as achieving a BMI of 18.5, a severely underweight patient who made significant increases in BMI yet did not meet the 18.5 threshold may be considered unsuccessful in treatment, despite making greater headway during treatment in terms of BMI increase than his or her less severely underweight counterparts. Further, certain studies include only more severe patients whereas others include much milder presentations, which may render cross-comparison difficult. Issues pertaining to range of presentation and severity may best be overcome by ensuring clinical presentation is adequately assessed and described, so that patients with vastly different presentations are less likely to be grouped together in analysis, and clinical presentation within the sample can be considered upon interpreting the results.

Further issues warranting mention are those of a statistical nature. Firstly, Due to the relatively low prevalence of anorexia, as well as high drop-out rates during treatment, large samples in empirical studies are often difficult to obtain. Thus, the majority of current studies may be afflicted by low power, and perhaps lack of significant findings, or failure to replicate previously identified significant findings, can often be explained by type II errors in the current literature. The implication for future research is in this case both obvious yet difficult to execute; larger samples are required if the relationship between pre-treatment predictors and drop-out and outcome in AN treatment is to be properly elucidated. The best way to achieve this is likely to be using carefully designed multi-centre studies. Moreover, as meeting eligibility criteria for the meta-analyses necessitated sufficient data be provided (either via the paper or via the authors) to allow a “clean” effect size to be determined (wherein a “clean” effect size refers to the effect of

a variable irrespective of other variables, , a number of papers were excluded due to missing data. Most frequently, data pertaining to insignificant findings, or data pertaining to “clean” effect sizes (e.g. correlations coefficients between the predictor and outcome calculated in order to determine eligibility for inclusion in multiple regression analysis) were frequently omitted. Specifically, As such, it is recommended that future studies present such data to allow comparison of effects across studies. Furthermore, considering that the overall effect sizes for pre-treatment predictors of drop-out and outcome identified so far is small, it is possible that identifying and quantifying pre-treatment factors is not particularly informative in predicting drop-out and outcome in treatment for AN. As such, reviewing the importance of factors measured early in therapy as opposed to at baseline (such as rate of weight gain or therapeutic alliance) may be worth examining in future research. Moreover, considering the small effect of pre-treatment patient variables investigated so far, previously unexamined pre-treatment patient variables, particularly those related to motivation, such as egosyntonicity (the degree to which patients value their disorder), may be worth examining.

References

- Abd Elbaky, G. B., Hay, P. J., le Grange, D., Lacey, H., Crosby, R. D., & Touyz, S. (2014). Pre-treatment predictors of attrition in a randomised controlled trial of psychological therapy for severe and enduring anorexia nervosa. *BMC Psychiatry*, 14, 69. doi:10.1186/1471-244x-14-69
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: American Psychiatric Association.
- Bachner-Melman, R., Zohar, A. H., & Ebstein, R. P. (2006). An examination of cognitive versus behavioral components of recovery from anorexia nervosa. *J. Nerv. Ment. Dis.*, 194(9), 697-703. doi:10.1097/01.nmd.0000235795.51683.99
- Bewell, C. V., & Carter, J. C. (2008). Readiness to change mediates the impact of eating disorder symptomatology on treatment outcome in anorexia nervosa. *Int. J. Eat. Disord.*, 41(4), 368-371. doi:10.1002/eat20513
- Birmingham, C. L., Touyz, S., & Harbottle, J. (2009). Are anorexia nervosa and bulimia nervosa separate disorders? Challenging the 'transdiagnostic' theory of eating disorders. *Eur. Eat. Disord. Rev.*, 17(1), 2-13. doi:10.1002/erv.896
- Bulik, C. M., Berkman, N. D., Brownley, K. A., Sedway, J. A., & Lohr, K. N. (2007). Anorexia nervosa treatment: a systematic review of randomized controlled trials. *Int. J. Eat. Disord.*, 40(4), 310-320. doi:10.1002/eat.20367
- Calugi, S., El Ghoch, M., Conti, M., & Dalle Grave, R. (2014). Depression and treatment outcome in anorexia nervosa. *Psychiatry Res.*, 218(1-2), 195-200. doi:10.1016/j.psychres.2014.04.024
- Carter, J. C., Bewell, C., Blackmore, E., & Woodside, D. B. (2006). The impact of childhood sexual abuse in anorexia nervosa. *Child Abuse Negl.*, 30(3), 257-269. doi:10.1016/j.chiabu.2005.09.004
- Carter, J. C., Blackmore, E., Sutandar-Pinnock, K., & Woodside, D. B. (2004). Relapse in anorexia nervosa: a survival analysis. *Psychol. Med.*, 34(4), 671-679. doi:10.1017/s0033291703001168
- Carter, J. C., Mercer-Lynn, K. B., Norwood, S. J., Bewell-Weiss, C. V., Crosby, R. D., Woodside, D. B., & Olmsted, M. P. (2012). A prospective study of predictors of relapse in anorexia nervosa: implications for relapse prevention. *Psychiatry Res.*, 200(2-3), 518-523. doi:10.1016/j.psychres.2012.04.037
- Cochran, W. G. (1954). The combination of estimates from different experiments. *Biometrics*, 10, 101-129. Retrieved from <http://www.jstor.org/stable/3001666>
- Dalle Grave, R., Calugi, S., Doll, H. A., & Fairburn, C. G. (2013). Enhanced cognitive behaviour therapy for adolescents with anorexia nervosa: an alternative to family therapy? *Behav. Res. Ther.*, 51(1), R9-r12. doi:10.1016/j.brat.2012.09.008
- DeJong, H., Broadbent, H., & Schmidt, U. (2012). A systematic review of dropout from treatment in outpatients with anorexia nervosa. *Int. J. Eat. Disord.*, 45(5), 635-647. doi:10.1002/eat.20956
- Doyle, P. M., Le Grange, D., Loeb, K., Doyle, A. C., & Crosby, R. D. (2010). Early response to family-based treatment for adolescent anorexia nervosa. *Int. J. Eat. Disord.*, 43(7), 659-662. doi:10.1002/eat.20764
- Dray, J., & Wade, T. D. (2012). Is the transtheoretical model and motivational interviewing approach applicable to the treatment of eating disorders? A review. *Clin. Psychol. Rev.*, 32(6), 558-565. doi:10.1016/j.cpr.2012.06.005

- Eivors, A., Button, E., Warner, S., & Turner, K. (2003). Understanding the experience of drop-out from treatment for anorexia nervosa. *European Eating Disorders Review*, 11(2), 90-107. doi:10.1002/erv.492
- El Ghoch, M., Calugi, S., Pellegrini, M., Milanese, C., Busacchi, M., Battistini, N. C., et al. (2013). Measured physical activity in anorexia nervosa: features and treatment outcome. *Int. J. Eat. Disord.*, 46(7), 709-712. doi:10.1002/eat.22140
- Fairburn, C. G., Cooper, Z., & Shafran, R. (2003). Cognitive behaviour therapy for eating disorders: a "transdiagnostic" theory and treatment. *Behav. Res. Ther.*, 41(5), 509-528.
- Fassino, S., Abbate Daga, G., Amianto, F., Leombruni, P., Garzaro, L., & Rovera, G. G. (2001). Nonresponder anorectic patients after 6 months of multimodal treatment: predictors of outcome. *Eur. Psychiatry*, 16(8), 466-473.
- Field, A. P. (2001). Meta-analysis of correlation coefficients: a Monte Carlo comparison of fixed- and random-effects methods. *Psychol. Methods*, 6(2), 161-180.
- Garfield, S. L. (1994). Psychotherapy: Then and now. *Clinical Psychology & Psychotherapy*, 1(2), 63-68. doi:10.1002/cpp.5640010202
- Teti, G. L., Rebok, F., Rojas, S. M., Grendas, L., & Daray, F. M. (2014). Systematic review of risk factors of suicide and suicide attempt among psychiatric patients in Latin America and Caribbean. *Revista Panamericana de Salud Publica*, 36(2), 124=133. Retrieved from https://scielosp.org/scielo.php?script=sci_arttext&pid=S1020-49892014000700008&lng=en&tlng=en
- Goddard, E., Hibbs, R., Raenker, S., Salerno, L., Arcelus, J., Boughton, N., et al. (2013). A multi-centre cohort study of short term outcomes of hospital treatment for anorexia nervosa in the UK. *BMC Psychiatry*, 13, 287. doi:10.1186/1471-244x-13-287
- Gowers, S. G., & Smyth, B. (2004). The Impact of a Motivational Assessment Interview on Initial Response to Treatment in Adolescent Anorexia Nervosa. *European Eating Disorders Review*, 12(2), 87-93. Retrieved from <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc4&AN=2004-13137-003>
- http://sfx.ucl.ac.uk/sfx_local?sid=OVID:psycdb&id=pmid:&id=doi:10.1002%2Ferv.555&issn=1072-4133&isbn=&volume=12&issue=2&spage=87&pages=87-93&date=2004&title=European+Eating+Disorders+Review&atitle=The+Impact+of+a+Motivational+Assessment+Interview+on+Initial+Response+to+Treatment+in+Adolescent+Anorexia+Nervosa.&aulast=Gowers
- Hall, S. M., & Brannick, M. T. (2002). Comparison of two random-effects methods of meta-analysis. *J. Appl. Psychol.*, 87(2), 377-389.
- Halmi, K. A. (2005). The multimodal treatment of eating disorders. *World Psychiatric Association*, 4(2), 66-73.
- Hartmann, A., Wirth, C., & Zeeck, A. (2007). Prediction of failure of inpatient treatment of anorexia nervosa with early weight gain. *Psychotherapy Res.*, 17, 218-229.
- Hartmann, A., Zeeck, A., & Barrett, M. S. (2010). Interpersonal problems in eating disorders. *International Journal of Eating Disorders*, 43(7), 619-627. doi:10.1002/eat.20747
- Hubert, T., Pioggiosi, P., Huas, C., Wallier, J., Maria, A. S., Apfel, A., et al. (2013). Drop-out from adolescent and young adult inpatient treatment for anorexia nervosa. *Psychiatry Res.*, 209(3), 632-637. doi:10.1016/j.psychres.2013.03.034
- Jarman, M., & Walsh, S. (1999). Evaluating recovery from anorexia nervosa and bulimia nervosa: integrating lessons learned from research and clinical practice. *Clin. Psychol. Rev.*, 19(7), 773-788.

- Jordan, J., McIntosh, V. V., Carter, F. A., Joyce, P. R., Frampton, C. M., McKenzie, J. M., et al. (2014). Clinical characteristics associated with premature termination from outpatient psychotherapy for anorexia nervosa. *Eur. Eat. Dis. Rev.*, 22(4), 278-284.
- Jüni, P., Altman, D. G., & Egger, M. (2001). Assessing the quality of controlled clinical trials. *BMJ*, 323, 42-46. doi:10.1136/bmj.323.7303.42
- Kahn, C., & Pike, K. M. (2001). In search of predictors of dropout from inpatient treatment for anorexia nervosa. *Int. J. Eat. Disord.*, 30(3), 237-244.
- Kastner, D., Gumz, A., Osen, B., Voderholzer, U., Wollburg, E., Karacic, M., . . . Lowe, B. (2015). Predictors of Outcome in Inpatients with Anorexia Nervosa: A Prospective Multi-Center Study. *Psychother. Psychosom.*, 84(4), 255-257. doi:10.1159/000381353
- Klump, K. L., Bulik, C. M., Pollice, C., Halmi, K. A., Fichter, M. M., Berrettini, W. H., . . . Kaye, W. H. (2000). Temperament and character in women with anorexia nervosa. *J. Nerv. Ment. Dis.*, 188(9), 559-567.
- Knowles, L., Anokhina, A., & Serpell, L. (2013). Motivational interventions in the eating disorders: what is the evidence? *Int. J. Eat. Disord.*, 46(2), 97-107. doi:10.1002/eat.22053
- Kordy, H., Kramer, B., Palmer, R. L., Papezova, H., Pellet, J., Richard, M., & Treasure, J. (2002). Remission, recovery, relapse, and recurrence in eating disorders: conceptualization and illustration of a validation strategy. *J. Clin. Psychol.*, 58(7), 833-846. doi:10.1002/jclp.2013
- Le Grange, D., Accurso, E. C., Lock, J., Agras, S., & Bryson, S. W. (2014). Early weight gain predicts outcome in two treatments for adolescent anorexia nervosa. *Int. J. Eat. Disord.*, 47(2), 124-129. doi:10.1002/eat.22221
- Le Grange, D., Fitzsimmons-Craft, E. E., Crosby, R. D., Hay, P., Lacey, H., Bamford, B., . . . Touyz, S. (2014). Predictors and moderators of outcome for severe and enduring anorexia nervosa. *Behav. Res. Ther.*, 56, 91-98. doi:10.1016/j.brat.2014.03.006
- Lock, J., Agras, W. S., Bryson, S. W., Brandt, H., Halmi, K. A., Kaye, W., . . . Jo, B. (2016). Does family-based treatment reduce the need for hospitalization in adolescent anorexia nervosa? *Int. J. Eat. Disord.*, 49(9), 891-894. doi:10.1002/eat.22536
- Lockwood, R., Serpell, L., & Waller, G. (2012). Moderators of weight gain in the early stages of outpatient cognitive behavioural therapy for adults with anorexia nervosa. *Int. J. Eat. Disord.*, 45(1), 51-56.
- Macdonald, P., Hibbs, R., Corfield, F., & Treasure, J. (2012). The use of motivational interviewing in eating disorders: a systematic review. *Psychiatry Res*, 200(1), 1-11. doi:10.1016/j.psychres.2012.05.013
- Mahon, J. (2000). Dropping out from psychological treatment for eating disorders: What are the issues? *European Eating Disorders Review*, 8(3), 198-216. Retrieved from <http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=psyc3&AN=2000-00010-002>
- Marcoulides, O. K., & Waller, G. (2012). Nonspecific predictors of weight gain in the early stages of outpatient cognitive behavioural therapy for adults with anorexia nervosa: Replication and extension. *Int. J. Eat. Disord.*, 45(6), 746-750.
- McHugh, M. D. (2007). Readiness for change and short-term outcomes of female adolescents in residential treatment for anorexia nervosa. *Int. J. Eat. Disord.*, 40(7), 602-612. doi:10.1002/eat20425
- Mewes, R., Tagay, S., & Senf, W. (2008). Weight curves as predictors of short-term outcome in anorexia nervosa inpatients. *Eur. Eat. Disord. Rev.*, 16(1), 37-43. doi:10.1002/erv.807
- Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J. Clin. Epidemiol.*, 62(10), 1006-1012. doi:10.1016/j.jclinepi.2009.06.005

- Olmos, M., Antelo, M., Vazquez, H., Smecuol, E., Maurino, E., & Bai, J. C. Systematic review and meta-analysis of observational studies on the prevalence of fractures in coeliac disease. *Digestive and Liver Disease*, 40(1), 46-53. doi:10.1016/j.dld.2007.09.006
- Pham-Scottet, A., Huas, C., Perez-Diaz, F., Nordon, C., Divac, S., Dardennes, R., . . . Rouillon, F. (2012). Why do people with eating disorders drop out from inpatient treatment?: the role of personality factors. *J. Nerv. Ment. Dis.*, 200(9), 807-813. doi:10.1097/NMD.0b013e318266bbba
- Rosenthal, R. (1979). The file drawer problem and tolerance for null results *Psychological Bulletin*, 86(3), 638-641. doi:10.1037/0033-2909.86.3.638
- Schnicker, K., Hiller, W., & Legenbauer, T. (2013). Drop-out and treatment outcome of outpatient cognitive-behavioral therapy for anorexia nervosa and bulimia nervosa. *Compr. Psychiatry*, 54(7), 812-823. doi:10.1016/j.comppsy.2013.02.007
- Sly, R. (2009). What's in a name? Classifying 'the dropout' from treatment for anorexia nervosa. *Eur. Eat. Disorders Rev.*, 17, 405-407. doi:10.1002/erv.964
- Sly, R., Morgan, J. F., Mountford, V. A., & Lacey, J. H. (2013). Predicting premature termination of hospitalised treatment for anorexia nervosa: the roles of therapeutic alliance, motivation, and behaviour change. *Eat. Behav.*, 14(2), 119-123. doi:10.1016/j.eatbeh.2013.01.007
- Speranza, M., Loas, G., Wallier, J., & Corcos, M. (2007). Predictive value of alexithymia in patients with eating disorders: a 3-year prospective study. *J. Psychosom. Res.*, 63(4), 365-371. doi:10.1016/j.jpsychores.2007.03.008
- Steinhausen, H. C. (2002). The outcome of anorexia nervosa in the 20th century. *Am. J. Psychiatry*, 159(8), 1284-1293. doi:10.1176/appi.ajp.159.8.1284
- Surgenor, L. J., Maguire, S., & Beumont, P. J. V. (2004). Drop-out from inpatient treatment for anorexia nervosa: can risk factors be identified at point of admission? *European Eating Disorders Review*, 12(2), 94-100. doi:10.1002/erv.539
- Thaler, L., Israel, M., Antunes, J. M., Sarin, S., Zuroff, D. C., & Steiger, H. (2016). An examination of the role of autonomous versus controlled motivation in predicting inpatient treatment outcome for anorexia nervosa. *Int. J. Eat. Dis.*, 49(6), 626-629.
- Thomas, J. J., Vartanian, L. R., & Brownell, K. D. (2009). The relationship between Eating Disorder Otherwise Specified (EDNOS) and officially recognized eating disorders: Meta-analysis and implications for DSM. *Psychological Bulletin*, 135(2), 407-433. doi:10.1037/a0015326
- Vall, E., & Wade, T. D. (2015). Predictors of treatment outcome in individuals with eating disorders: A systematic review and meta-analysis. *Int. J. Eat. Disord.*, 48(7), 946-971. doi:10.1002/eat.22411
- Vitousek, K., Watson, S., & Wilson, G. T. (1998). Enhancing motivation for change in treatment-resistant eating disorders. *Clin. Psychol. Rev.*, 18(4), 391-420.
- Wade, T. D., Bergin, J. L., Tiggemann, M., Bulik, C. M., & Fairburn, C. G. (2006). Prevalence and long-term course of lifetime eating disorders in an adult Australian twin cohort. *Aust N Z J Psychiatry*, 40(2), 121-128. doi:10.1080/j.1440-1614.2006.01758.x
- Wales, J., Brewin, N., Cashmore, R., Haycraft, E., Baggott, J., Cooper, A., et al. (2016). Predictors of Positive Treatment Outcome in People With Anorexia Nervosa Treated in a Specialized Inpatient Unit: The Role of Early Response to Treatment. *Eur. Eat. Disord. Rev.*, 24(5), 417-424. doi:10.1002/erv.2443
- Wallier, J., Vibert, S., Berthoz, S., Huas, C., Hubert, T., & Godart, N. (2009). Dropout from inpatient treatment for anorexia nervosa: critical review of the literature. *Int. J. Eat. Disord.*, 42(7), 636-647. doi:10.1002/eat.20609

- Ward, A., Troop, N., Todd, G., & Treasure, J. (1996). To change or not to change--'how' is the question? *Br J Med. Psychol.*, 69 (Pt 2), 139-146.
- Wild, B., Friederich, H. C., Zipfel, S., Resmark, G., Giel, K., Teufel, M., . . . Herzog, W. (2016). Predictors of outcomes in outpatients with anorexia nervosa - Results from the ANTOP study. *Psychiatry Res.*, 244, 45-50. doi:10.1016/j.psychres.2016.07.002
- Wildes, J. E., Marcus, M. D., Crosby, R. D., Ringham, R. M., Dapelo, M. M., Gaskill, J. A., & Forbush, K. T. (2011). The clinical utility of personality subtypes in patients with anorexia nervosa. *J. Consult. Clin. Psychol*, 79(5), 665-674. doi:10.1037/a0024597
- World Health Organisation. (1992). *The ICD-10 classification of mental and behavioural disorders: Clinical descriptions and diagnostic guidelines*. Geneva: World Health Organisation.
- Zeeck, A., Hartmann, A., Buchholz, C., & Herzog, T. (2005). Drop outs from in-patient treatment of anorexia nervosa. *Acta Psychiatr. Scand.*, 111(1), 29-37. doi:10.1111/j.1600-0447.2004.00378.x
- Zipfel, S., Giel, K. E., Bulik, C. M., Hay, P., & Schmidt, U. (2015). Anorexia nervosa: aetiology, assessment, and treatment. *Lancet Psychiatry*, 2(12), 1099-1111. doi:10.1016/s2215-0366(15)00356-9

Acknowledgements

The authors wish to extend a special thank you to Dr. Lea Thealer, Dr. Daniel Le Grange, Dr. Ross Crosby, Dr. Stephen Touyz, and Dr. Deniese Kaestner for providing us with additional data necessary to complete our analyses.

Author disclosure

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.