Moderators of change in an Internet-based intervention for eating disorders with different levels of therapist support: What works for whom?

Jiska J. Aardoom¹, MSc
Alexandra E. Dingemans¹, PhD
Marjolein Fokkema², PhD
Philip Spinhoven^{2,3}, PhD
Eric F. Van Furth^{1,3}, PhD

- ¹ Rivierduinen Eating Disorders Ursula, Leiden, the Netherlands
- ² Institute of Psychology, Leiden University, Leiden, the Netherlands
- ³ Department of Psychiatry, Leiden University Medical Center, Leiden, the Netherlands

Address correspondence and reprint requests to:

Alexandra E. Dingemans

Rivierduinen Eating Disorders Ursula

P.O. Box 405

2300 AK Leiden

The Netherlands

Tel: +31 71 890 3344

E-mail: a.dingemans@rivierduinen.nl

Abstract

This study investigated moderators of intervention response in a fully automated Internet-based monitoring and feedback intervention ('Featback') with different levels of therapist support for individuals with eating disorder (ED) symptoms. This study was part of a randomized controlled trial comparing four conditions: 1) Featback, 2) Featback with low-intensity (weekly) therapist support, 3) Featback with high-intensity (three times a week) therapist support, and 4) a waiting list. A total of 273 participants completed baseline and post-intervention assessments. The outcome measure was ED psychopathology. Model-based recursive partitioning was applied. Baseline levels of ED psychopathology were found to moderate intervention response. Specifically, in terms of improvement in symptoms of anorexia nervosa, participants with higher baseline levels of anorectic psychopathology showed better outcomes in the waiting list condition and the Featback conditions with low- and high-intensity therapist support in comparison with Featback without therapist support. In terms of improvement in symptoms of bulimia nervosa, participants with mild to moderate bulimic symptoms had better outcomes in the Featback conditions compared with the waiting list. Thus, the fully automated Internet-based intervention with and without therapist support may be particularly suitable in improving mild to moderate bulimic psychopathology, whereas the intervention without therapist support may be less effective in improving severe anorectic psychopathology. Further investigating differential intervention responses is important, as this could help to optimize the delivery and dissemination of E-health interventions and therapist support, which in turn could help moving toward personalized (E-)care.

Keywords: E-health; Internet-based; Eating disorders; Anorexia nervosa; Bulimia nervosa; Therapist support; Moderators

Introduction

Numerous studies have demonstrated that Internet-based interventions can reduce eating disorder (ED) psychopathology (e.g. (Aardoom, Dingemans, Spinhoven, & van Furth, 2013; Beintner, Jacobi, & Taylor, 2011; Melioli et al., 2016). However, investigating the average impact of Internet-based interventions could mask individual differences in responses to such interventions. Little is known about patient characteristics that may be relevant for predicting who will benefit from such interventions and who will not. It is possible that certain subgroups of participants respond better to particular Internet-based interventions than others. In addition, there may be differences in the way specific subgroups of patients respond to therapist contact. Moderator analyses can be used to investigate such individual differences in intervention response (Baron & Kenny, 1986; Frazier, Tix, & Barron, 2004; Kraemer, Wilson, Fairburn, & Agras, 2002), specifying for whom and under what conditions an intervention is effective. Moderators are baseline variables that are associated with intervention outcome, where the magnitude or direction of the effect differs across interventions (e.g. if women do better in intervention X, whereas men do better in intervention Y). General predictor variables differ from moderator variables in that the association of the predictor with intervention outcome does not differ across interventions (e.g. if women respond better than men to both intervention X and intervention Y).

The current study focused on detecting moderators of intervention response which could be highly informative for clinical practice. Identifying who will do best with which kind of intervention could optimize the delivery and dissemination of an intervention by tailoring the type and intensity of the intervention to individual patient characteristics. It is a first step toward the development of personalized patient care. Personalized care is becoming increasingly important and is preferable to a 'one-size-fits-all' approach. Indeed, for adults with anorexia nervosa, there is no single superior treatment approach (National Institute for Clinical Excellence, 2004), and for individuals with bulimia nervosa and binge-eating disorder, the treatment of choice (i.e. cognitive behavioral therapy) still fails to help a substantial proportion of patients (Wilson, Grilo, & Vitousek, 2007).

Numerous studies have identified general predictors of outcome for individuals with ED in naturalistic settings, face-to-face treatments, and E-health interventions (Berkman, 2007; Wagner et al., 2015; Grilo, Masheb, & Crosby, 2012; Fichter, Quadflieg, & Hedlund, 2006; Keel & Brown, 2010). Higher motivation to change and drive for thinness, and lower levels of binge eating and body dissatisfaction, were found to be associated with better outcomes (Wagner et al., 2015). With respect to body mass index (BMI) as predictor of outcome, results have demonstrated mixed results: one study found an Internet-based intervention to be more beneficial for participants with an elevated baseline BMI (Taylor et al., 2006), whereas two other studies demonstrated greater effects for participants with

a lower baseline BMI (Hogdahl, Birgegard, & Bjorck, 2013). The type of eating disorder symptoms have also been found to predict participants' outcome in Internet-based interventions. More specifically, Ljotsson et al. (2007) found that participants with binge eating disorder improved to a greater extent than participants with bulimia nervosa, and a study by Jacobi et al. (2011) showed better outcomes for participants who demonstrated binge eating episodes and compensatory behaviors as compared to those with restrictive eating as their sole symptom of disordered eating. Finally, one study (Carrard et al., 2011; Carrard et al., 2011) evaluated an online guided self-help program across several European countries and demonstrated that better psychological health and less comorbid psychopathology predicted greater improvements in symptoms of bulimia nervosa. Keel et al. (2010) reviewed the literature with respect to prognostic factors for ED course and outcome. Factors related to the severity and duration of the illness were identified as negative predictors of outcome for individuals with anorexia nervosa. For individuals with bulimia nervosa, greater psychiatric comorbidity was found to predict poorer outcomes, whereas for binge-eating disorder and eating disorder not otherwise specified, few prognostic factors could be reliably identified.

Research into moderators of intervention response within face-to-face or E-health settings is scarce. To date, two studies have compared face-to-face prevention programs for ED with an educational brochure or assessment-only control condition respectively. Stronger intervention effects were found for those with elevated baseline levels of ED symptoms (Stice, Rohde, Shaw, & Marti, 2013; Stice, Rohde, Shaw, & Marti, 2012), and higher levels of body image distress, bulimic symptoms, and thin-ideal internalization (Stice, Marti, Shaw, & O'Neil, 2008). Taylor et al. (2006) investigated moderators of outcome in a randomized controlled trial comparing an Internet-based prevention program with a waiting list control condition. Participants with an elevated baseline BMI of > 25 and a higher baseline frequency of compensatory behaviors achieved significantly better outcomes in the intervention condition compared with the waiting list condition. Finally, a study by Völker et al. (2014) identified several moderators of response in a similar Internet-based prevention program. They found that reductions in binge-eating were stronger for participants with a lower BMI and a higher frequency of purging at baseline. In terms of moderators of outcome as defined by general levels of ED psychopathology, those who restricted their caloric intake and showed lower levels of purging at baseline had a better outcome (Volker, Jacobi, Trockel, & Taylor, 2014). In sum, there is only limited and conflicting evidence regarding moderators of intervention outcomes for individuals with ED symptoms.

The role of therapist support within E-health interventions is an important factor to consider when studying the effectiveness of an intervention and moderators of intervention response. In the field of depression and anxiety, two meta-analyses have found that Internet-based interventions with therapist support were more effective than those without or those with only minimal therapeutic

contact (Andersson & Cuijpers, 2009; Spek et al., 2007). However, direct comparisons of E-health interventions with and without therapist support in randomized controlled trials are scarce, and studies investigating the optimal intensity of therapist support are rare (Baumeister, Reichler, Munzinger, & Lin, 2015). The question of whether a particular Internet-based intervention with therapist support is more effective in comparison to the same intervention without therapist support, and exploring for whom (i.e., which subgroups of participants) this is true, warrants further investigation. For example, one might hypothesize that adding therapist support could be more effective for individuals with a longer illness duration or higher symptom severity, given that these patients are in higher need of specialized support.

The aim of this explorative study was to examine moderators of outcome in a fully automated Internet-based monitoring and feedback intervention ('Featback'), supplemented with different intensities of therapist support (i.e. none, once a week, and three times a week) for individuals with ED symptoms. This could help to identify patients who are likely to benefit from Featback and additional therapist support, and patients who are not. A selection of potential moderators of change in ED psychopathology was tested based on theory and previous research in the field of E-health programs targeting ED psychopathology, as well as in the field of ED more generally. The selection of moderators included socio-demographical characteristics (age (Berkman, 2007) and education level (Wilson, Wilfley, Agras, & Bryson, 2010)), clinical characteristics (baseline levels of ED psychopathology (Fernández-Aranda et al., 2009; Hilbert & Tuschen-Caffier, 2007; Volker et al., 2014; Wagner et al., 2013; Wilson et al., 2010) and body mass index (Hogdahl et al., 2013; Taylor et al., 2006; Volker et al., 2014), comorbid symptoms of anxiety and depression (Berkman, 2007; Carrard et al., 2011; Fichter, Quadflieg, & Hedlund, 2008; Keel et al., 2010), levels of perseverative thinking (Warmerdam, van, Jongsma, Twisk, & Cuijpers, 2010), treatment status (Keel et al., 2010), the duration of ED psychopathology (Keel et al., 2010), and ED subtype (Jacobi, Völker, Trockel, & Taylor, 2011; Ljotsson et al., 2007; Volker et al., 2014), as well as motivational variables (i.e. perceived importance, readiness, and ability to change) (Dingemans et al., 2014; Steele, Bergin, & Wade, 2011; Wade, Frayne, Edwards, Robertson, & Gilchrist, 2009; Wagner et al., 2015; Wolk & Devlin, 2001).

Method

Study design and participants

This study was conducted as part of a randomized controlled trial (Aardoom, Dingemans, Spinhoven, Roijen, & van Furth, 2013). This trial involved four conditions: 1) 'Featback', an Internet-based self-help intervention for individuals with ED symptoms, consisting of psychoeducation and a fully automated

monitoring and feedback system, 2) Featback supplemented with the possibility of low-intensity (weekly) therapist support by means of e-mail, chat, or Skype, 3) Featback supplemented with the possibility of high-intensity (three times a week) therapist support, and 4) a waiting list control condition. The fully automated monitoring and feedback system comprised a weekly monitoring questionnaire addressing ED psychopathology. After completion of this questionnaire, supportive feedback messages were automatically generated according to a pre-defined algorithm and sent to the participants accordingly (for more details on the study design and the intervention, see Aardoom et al. (2013)).

Participants (N=354) were recruited via the Featback website and the website (http://www.proud2bme.nl) of a Dutch pro-recovery focused e-community for young women with ED problems. The eligibility criteria were 1) age ≥ 16 , 2) access to the Internet, and 3) self-reported ED symptoms. Ethical approval for the study was obtained from the Leiden University Medical Center ethics committee. The results of this randomized controlled trial demonstrated that Featback was superior in reducing bulimic psychopathology, symptoms of depression and anxiety, and levels of perseverative thinking, in comparison with the waiting list (Aardoom et al., 2016). Contrary to the expectations, no added value of therapist support was found in terms of the effectiveness of Featback.

The current study only included the data of participants who completed both baseline and post-intervention assessments (n=273).

Outcome variables

Outcome variables were assessed at baseline and post-intervention, and included anorectic and bulimic psychopathology as measured by the Short Evaluation of Eating Disorders (SEED) (Bauer, Winn, Schmidt, & Kordy, 2005). The SEED is a brief self-report measure for the assessment of core eating disorder symptoms over the past week. The SEED assesses the main symptoms of anorexia nervosa (underweight, fear of weight gain, distortion of body perception) and bulimia nervosa (binge-eating, compensatory behaviors, over-concern with body shape and weight). Total severity indexes can be calculated for each of these two dimensions (range 0–3), with higher scores reflecting higher severity indexes. The SEED has demonstrated construct, discriminative, and concurrent validity, and has shown that it is sensitive to symptom change (Bauer et al., 2005).

Potential moderator variables

Socio-demographic variables

Socio-demographic variables included as potential moderator variables were age and level of education (low, medium, high).

Eating disorder psychopathology

Potential moderator variables related to eating disorder psychopathology included baseline levels of anorectic and bulimic psychopathology (SEED), treatment history (yes/no), duration of ED problems (years), and BMI (underweight (<18.5), healthy weight (18.5-25), overweight (25-30), and obese (>30)). Finally, ED type (anorexia nervosa, binge-eating disorder, bulimia nervosa, purging disorder, and unspecified feeding or ED or an ED problem) was assessed by the Eating Disorder Examination Questionnaire (EDE-Q) (Fairburn & Beglin, 2008). The EDE-Q is a widely used self-report questionnaire that assesses both the core attitudinal features of ED psychopathology and the frequency of core ED behaviors over the past 28 days. The EDE-Q has demonstrated test-retest and internal consistency reliability, as well as criterion-oriented and construct validity (Berg, Peterson, Frazier, & Crow, 2011). The internal consistency reliability in the current sample was high (Cronbach's α =.90). On the basis of the EDE-Q, the participants were classified into five ED categories according to the criteria of the DSM-5 (American Psychiatric Association, 2013). Participants who reported a body mass index of ≤ 18.5 combined with a fear of weight gain or of becoming fat were classified as anorexia nervosa. Participants were classified in the binge-eating disorder category if they reported objective bingeeating episodes at least once a week in the past 28 days, without recurrent use of inappropriate compensatory behaviors (i.e. less than once a week over the past 28 days). The category of bulimia nervosa consisted of participants with self-reported episodes of objective binge-eating and inappropriate compensatory behaviors (i.e. self-induced vomiting or misuse of laxatives), both at least once a week or more during the past 28 days. The purging disorder category comprised participants who self-reported purging behaviors once a week or more during the past 28 days in the absence of binge-eating episodes. Finally, if participants did not meet the criteria of any of the categories mentioned above, they were categorized under an unspecified feeding or ED or an ED problem without a DSM-5 classification.

Motivation to change

Three motivation rulers were used to assess participants' motivation to change: their perceived importance of change, their perceived ability/confidence to change, and their perceived readiness to change. Such rulers have been used in previous studies in the field of eating disorders (Bewell & Carter, 2008; Genders & Tchanturia, 2010; Weiss, Mills, Westra, & Carter, 2013), and have demonstrated good psychometric properties in the field of smoking cessation (Boudreaux et al., 2012). Responses were scored on an 11-point Likert scale, ranging from 0 'not at all' to 10 'very much'.

Symptoms of anxiety and depression

The 4-item Patient Health Questionnaire (PHQ-4) (Kroenke, Spitzer, Williams, & Löwe, 2009) assesses symptoms of anxiety and depression over the past 2 weeks. The PHQ-4 comprises two core anxiety items and two core depression items, all of which can be answered on a 4-point Likert scale, ranging from 0 'not at all' to 3 'nearly every day'. A total score (range 0–12) can be calculated by summing the scores of all four items, with higher scores reflecting higher symptom severity. Factorial and construct validity have been demonstrated by Kroenke et al. (2009). The internal consistency reliability in the current sample was high (Cronbach's α =.83).

Levels of perseverative thinking

The 15-item Perseverative Thinking Questionnaire (PTQ) (Ehring, Raes, Weidacker, & Emmelkamp, 2012) was used as a global measure of repetitive negative thinking in the form of content-independent worry and rumination. The PTQ assesses the repetitiveness, intrusiveness, difficulties with disengagement from, and unproductiveness of repetitive negative thinking. It also assesses the degree to which it captures mental capacity. Items can be answered on a 5-point Likert scale, ranging from 0 'never' to 4 'almost always'. The timeframe was changed from 'in general' to 'in the previous 4 weeks'. The Dutch PTQ has demonstrated good internal consistency and satisfactory stability (Ehring et al., 2012). In the current study sample, the internal consistency reliability was high (Cronbach's α =.95).

Statistical analyses

All data were analyzed in R version 3.2.1 (R Development Core Team, 2014). Potential moderators were investigated using model-based recursive partitioning methods (Hothorn & Zeileis, 2015). Model-based recursive partitioning can be used to detect treatment-subgroup interactions: subgroups of individuals with different (i.e. more or less favorable) responses to one or more treatments, compared with other individuals (Doove, Dusseldorp, van Deun, & van Mechelen, 2014). In other words, treatment-subgroup interactions occur when subgroups of patients show differences in the effectiveness of one or more treatments. In treatment-subgroup interaction analyses, these subgroups are induced based on pre-treatment patient characteristics, a variable quantifying treatment response and a treatment indicator. Translated to the current study, this means investigating which subgroups of patients respond best to 1) Featback without therapist support, 2) Featback with low-intensity (i.e. weekly) therapist support, 3) Featback with high-intensity (i.e. three times a week) therapist support, or 4) a waiting list control condition (i.e. usual care). Advantages of model-based recursive partitioning methods include the ability to handle many potential moderator variables at once in one model, the

modeling of non-linear relationships, and the ability to capture (higher-order) interaction effects between predictor variables. They also provide specific cut-off ('split') points for the moderator variables, which facilitates the identification of subgroups that are likely to respond or not. In addition, the results of model-based recursive partitioning can be graphically represented as a decision tree. These trees are more easily interpretable than the outcomes of linear models, and can be used directly as a decision-making tool in clinical practice (Fokkema, Smits, Kelderman, & Penninx, 2015; Martignon, Vitouch, Takezawa, & Forster, 2003).

The model-based recursive partitioning algorithm (Zeileis, Hothorn, & Hornik, 2008) cycles interactively through the following steps: (1) fit a parametric model to the dataset, (2) test for parameter stability over a set of partitioning variables, (3) if there is some overall parameter instability, split the dataset with respect to the variable associated with the highest instability, (4) repeat the procedure in each of the resulting subgroups. In the current study, the parametric model in step (1) of the algorithm is a linear model, in which treatment outcome is regressed on intervention type. Treatment outcome was operationalized as change in outcome, calculated as post-intervention scores minus baseline scores, so that a negative score represented a reduction in ED psychopathology. The set of partitioning variables from step (2) have been described above, in the subsection 'Potential moderator variables'. The parameter stability tests used in this step of the algorithm are described in more detail in Zeileis (2015). In step (3), if one of the partitioning variables has a *p*-value for the instability test below the pre-specified alpha value (.05 in the current study), the partitioning variable with the lowest *p*-value is selected. The selected splitting value for that variable is taken to be the value that minimizes the sum of the sum of squares in both partitions.

In applying the model-based recursive partitioning algorithm, default settings of the Imtree function of the party kit were used for all analyses. More specifically, the alpha level for the parameter stability tests was set to .05, and the Bonferroni was applied to correct for multiple testing (the Bonferroni corrected p-value is calculated as $1-(1-p_j)^m$, where m is the number of partitioning covariates and p_j . is the original p-value of variable j).

In line with the conducted analyses regarding the effectiveness of Featback (Aardoom et al., 2016), in the model-based recursive partitioning analyses, we first compared the waiting list control condition with the three pooled Featback conditions. After this, the Featback conditions were compared individually, and with the waiting list control condition. Between-group effect sizes were calculated by dividing the sum of the means of both conditions by the pooled standard deviation of the samples at baseline.

Results

Participants

A total of 273 (77.1%, dropout=22.9%) participants provided data at baseline and post-intervention: 60 (60.9%) participants in the Featback condition, 70 (79.5%) and 71 (79.8%) participants in the Featback condition supplemented with low-and high-intensity therapist support respectively, and 72 (80.0%) participants in the waiting list control condition. Study dropout rates did not significantly differ between conditions at post-intervention ($\chi^2(3)$ =4.35, p=.23). No significant baseline differences were found between dropouts and completers regarding baseline demographic and clinical characteristics (i.e. age, level of education, duration ED psychopathology; all p > 0.5), nor on the outcome variable or any of the potential moderator variables: all p > 0.5.

The baseline characteristics of the study population are presented in Table 1. Participants were mainly female (n=271, 99.3%) and had a mean age of 24.4 years. Approximately 48.9% of the participants reported to have been diagnosed with an ED. Participants demonstrated severe levels of ED psychopathology as measured by the EDE-Q (M=4.1, SD=0.9). More specifically, the mean EDE-Q score is comparable to the overall norm for treatment-seeking patients with an ED in our specialized ED program (Aardoom, Dingemans, Slof Op't Landt, & van Furth, 2012), and approximately 97.6% of the study participants scored above the clinical significance cut-off point of 2.2 (Dingemans et al., 2016). No significant differences were found between the four study conditions on any of the potential moderator and outcome variables at baseline (all p>0.5).

Moderators

Anorectic psychopathology

Figure 1 shows the results of the model-based recursive partitioning analysis with change in anorectic psychopathology as outcome measure. Of all entered potential moderator variables, only baseline symptoms of anorexia nervosa were found to significantly moderate intervention response. More specifically, as can be seen at the upper end of Figure 1, the variable was split at values equal to or lower than 1.5 (subgroup 1, n=217) and higher than 1.5 (subgroup 2, n=47). These subgroups consisted of participants with relatively low and high baseline levels of anorectic psychopathology respectively. For participants with relatively low levels of baseline anorectic psychopathology, the effects of both Featback and the waiting list were very small or negligible. More specifically, neither the Featback nor the waiting list appeared to be effective in reducing anorectic psychopathology. At the end of the 8-week intervention, a small increase of 0.06 in anorectic psychopathology as measured by the SEED was found for the waiting list and an increase of 0.02 for the pooled Featback conditions (Cohens' d=0.10, 95%Cl=-0.01 to 0.16). At the bottom of Figure 1, the results are further specified for the individual

Featback conditions with different levels of therapist support. For individuals with low baseline levels of anorectic psychopathology, there was a small increase in symptoms for participants who received Featback without therapist support (0.02) and Featback with low-intensity therapist support (0.10), while there was a small reduction in symptoms in the Featback condition with high-intensity therapist support (-.05).

For participants with relatively high levels of baseline anorectic psychopathology (subgroup 2), small differences between the waiting list and the Featback conditions (Cohens' d=-0.25, 95%Cl=-0.48 to -0.12) were found regarding change in anorectic psychopathology. More specifically, the decrease in anorectic psychopathology was slightly higher in the waiting list condition (-0.22) than in the Featback conditions (-0.12). Further comparison of the three Featback conditions revealed reductions in anorectic psychopathology in the Featback conditions with low- (-0.18) and high-intensity therapist support (-0.13), whereas no change was found for participants who received Featback without therapist support (0.00). The differences between Featback without therapist support and Featback with low-intensity (Cohens' d=0.46, 95%Cl=0.23 to 0.69) and high-intensity therapist support (Cohens' d=0.31, 95%Cl=0.07 to 0.54) were small. Finally, the difference between Featback with low- and high-intensity therapist support was negligible (Cohens' d=-0.15, 95%Cl=-0.38 to -0.08).

Bulimic psychopathology

Only baseline symptoms of bulimia nervosa were found to significantly moderate intervention response in terms of reduction in bulimic psychopathology (see Figure 2). For participants with relatively low levels of bulimic psychopathology (i.e. subgroup 1 (n=163), SEED-BN \leq 1.5), a significant difference of moderate strength (Cohens' d=0.51, 95%C/=0.30 to 0.63) was found regarding change over time in bulimic psychopathology. As shown in Figure 2, participants in the Featback conditions displayed a reduction in bulimic psychopathology (-0.06) whereas participants in the waiting list control condition displayed an increase in symptoms (0.28). The results for the individual Featback conditions are presented at the bottom of Figure 2, and show that for individuals with relatively low levels of bulimic psychopathology, the decrease in symptoms is roughly similar: -0.06 for individuals who received Featback without therapist support, and -0.04 and -0.07 for participants who received Featback with low- and high-intensity therapist support respectively.

The results of participants with relatively high bulimic psychopathology (i.e. subgroup 2 (n=105), SEED-BN > 1.5) are shown on the right-hand side of Figure 2. The decrease in bulimic symptoms was very similar between the waiting list and the pooled Featback conditions: -0.32 and -0.31 respectively (Cohens' d=-0.02; 95%Cl=-0.27 to 0.13). In addition, the decrease in bulimic psychopathology was somewhat lower for individuals who received Featback without therapist

support (-0.23), and somewhat higher for participants who received Featback with low- (-0.38) and high-intensity (-0.31) therapist support respectively.

Discussion

The current study aimed to investigate moderators of response in a fully automated Internet-based monitoring and feedback intervention ('Featback') with different levels of therapist support (i.e. none, once a week, three times a week) as compared with a waiting list for individuals with ED symptoms. The results suggested that offering a fully automated monitoring and feedback system and/or therapist support to individuals who experience mild to moderate anorectic psychopathology seems to have no added value in terms of improvement in symptoms of anorexia nervosa. For those with relatively severe anorectic psychopathology, Featback with supplemental therapist support resulted in symptom reductions similar to those of usual care, while Featback without therapist support is perhaps inadvisable. With regard to bulimic psychopathology, participants with relatively high bulimic symptoms showed similar reductions across all four conditions, whereas participants with relatively less severe bulimic symptoms had a better outcome in the Featback conditions as compared with usual care in terms of improvement in symptoms of bulimia nervosa. The results therefore suggest that Featback with and without therapist support is particularly useful in improving mild to moderate bulimic psychopathology, whereas Featback without therapist support may be less suitable in improving severe anorectic psychopathology

Featback was superior to usual care for individuals with mild to moderate bulimic psychopathology in reducing symptoms of bulimia nervosa, but not for individuals with mild to moderate anorectic psychopathology in reducing symptoms of anorexia nervosa. A possible explanation might be that binge-eating behaviors and compensatory behaviors are somewhat less difficult to target and change than core anorectic psychopathological beliefs and underweight. In other words, the binge-eating and compensatory behaviors can be more ego-dystonic in nature than, for example, the more ego-syntonic restrictive symptoms of anorexia nervosa (Schmidt & Treasure, 2006). Binge-eating and compensatory behaviors are often accompanied by shame and perceived as problematic and incongruent with the self, hence individuals may have more motivation to change these behaviors.

The automated monitoring and feedback system without therapist support was not found to be effective in improving high levels of anorectic psychopathology. Presumably, the automated feedback messages are insufficient to help them in dealing with their symptoms. It is possible that in this case, it is de-motivating for participants to keep getting feedback messages with concerns about their wellbeing, without sufficient counseling in dealing with these concerns. Although adding

supplemental therapist support did increase the effectiveness of the intervention, Featback with therapist support was not found to be more effective than usual care.

The results suggest that a fully automated monitoring and feedback system may be particularly suitable in improving mild to moderate bulimic psychopathology, however adding supplemental therapist support did not increase the effectiveness of the intervention for individuals with mild to moderate bulimic symptoms. This is in line with the findings of Kelders et al. (2015), who demonstrated that a web-based intervention for individuals with mild to moderate depressive symptoms resulted in similar effectiveness at 6-month follow-up when provided with human support or automated support. Although the potential of automated support should be further investigated, preliminary results suggest that automated support can be an effective way of supporting individuals with mild to moderate bulimic psychopathology in the context of an Internet-based intervention. Hence, providing automated support might reduce the need for human therapist support, at least to some extent. If so, this could have important implications for the implementation of such interventions, potentially increasing the availability of health care services and making it possible to reach more individuals.

Given that symptoms of anorexia nervosa and bulimia nervosa are not independent and can co-occur, the implications of our current findings should always be considered in the context of the combination of these symptoms. For example, for individuals with mild anorectic psychopathology and mild bulimic psychopathology, one might offer Featback with or without support considering that this is more effective than a waiting list in improving symptoms of bulimia nervosa. For individuals with severe anorectic psychopathology and mild bulimic psychopathology, one might offer Featback with therapist support considering that this is more effective than Featback without therapist support with respect to improving severe symptoms of anorexia nervosa. For individuals with severe bulimic psychopathology and mild anorectic psychopathology, our preliminary results suggest that Featback with and without therapist support is just as effective as a waiting list, hence there is no preference for one of the four strategies. Therefore, Featback should not be offered. Finally, for individuals with severe bulimic psychopathology and severe anorectic psychopathology, one might offer Featback with therapist support considering that this is more effective than Featback without therapist support with respect to improving severe anorectic symptoms.

Numerous variables other than baseline ED psychopathology were found not to moderate intervention response. This suggests that Featback can be effective for a broad population of individuals experiencing symptoms of bulimia nervosa, irrespective of socio-demographic variables, comorbid symptoms, level of motivation to change, duration of ED symptoms, and whether the individual has received treatment or is currently receiving treatment. These last findings are particularly interesting, as they could imply that a fully automated Internet-based intervention can provide effective care for individuals with ED symptoms during various stages of their disorder, either

as a stand-alone health care service, as an adjunct to usual care, or possibly as part of a stepped-care program for the treatment of ED.

This study has several strengths and limitations. One limitation was that only moderators of short-term intervention response from baseline to post-intervention were investigated. It is not known whether the results will generalize to longer periods of follow-up. In addition, the analyses were restricted to completers of both baseline and post-intervention assessments. Although we identified significant moderator effects, the results should be interpreted with caution. In the field of ED our study is the first to study moderators of intervention response using recursive partitioning methods, although these methods have been used to identify risk factors of the onset of ED psychopathology (Jacobi et al., 2011; Stice, Marti, Spoor, Presnell, & Shaw, 2008; Stice, Marti, & Durant, 2011). Recursive partitioning methods are a promising approach for detecting moderators of intervention response. The results can easily be translated into clinical practice, since relevant patient characteristics and cutoff scores are identified. However, model-based recursive partitioning is an exploratory approach and confirmatory studies would be of great interest. Moreover, the subgroup of participants with high anorectic psychopathology was relatively small. Further studies and replication studies are therefore needed before the results of this study can be generalized to other eating disordered populations. Finally, the decision tree resulting from the moderator analyses should first be validated before being used in clinical practice to guide the selection of tailored interventions and therapist support. Ideally, our results should be tested in a randomized controlled trial with stratification based on severity levels of anorectic and bulimic psychopathology, as relevant. It would also be interesting to investigate potential moderator effects in different contexts. For example, Featback as an add-on to usual care as compared with usual care alone, or Featback as part of a first step in a stepped-care treatment for eating disorders as compared with treatment in the usual way.

In sum, our preliminary results suggest that a fully automated Internet-based monitoring and feedback system may be particularly suitable for individuals with mild to moderate bulimic psychopathology. The detection of subgroups of patients showing differential intervention responses is an important direction for future research, as it could help to optimize the delivery and dissemination of E-health interventions and therapist support, which in turn could help moving toward personalized (E-)care.

Acknowledgements

This study was part of a randomized controlled trial that was supported by a grant from the European Commission's in the Health Program (Contract No: 20101209).

Reference List

Aardoom, J. J., Dingemans, A. E., Slof Op't Landt, M. C., & van Furth, E. F. (2012). Norms and discriminative validity of the Eating Disorder Examination Questionnaire (EDE-Q). *Eating Behaviors*, 13, 305-309.

Aardoom, J. J., Dingemans, A. E., Spinhoven, P., Roijen, L. H., & van Furth, E. F. (2013). An Internet-based intervention for eating disorders consisting of automated computer-tailored feedback with or without supplemented frequent or infrequent support from a coach: study protocol for a randomized controlled trial. *Trials*, 14, 340.

Aardoom, J. J., Dingemans, A. E., Spinhoven, P., & van Furth, E. F. (2013). Treating eating disorders over the internet: a systematic review and future research directions. *Int J Eat Disord, 46,* 539-552.

Aardoom, J., Dingemans, A., Spinhoven, P., van Ginkel, J., de Rooij, M., & van Furth, E. (2016). Internet-based fully automated self-help with different levels of therapist support for individuals with eating disorder symptoms: A randomized controlled trial. *Journal of Medical Internet Research*, 17;18(6):e159.

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders (5th ed.).* (5th ed.) Washington, DC.

Andersson, G. & Cuijpers, P. (2009). Internet-based and other computerized psychological treatments for adult depression: A meta-analysis. *Cognitive Behaviour Therapy, 38,* 196-205.

Baron, R. M. & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology*, *51*, 1173-1182.

Bauer, S., Winn, S., Schmidt, U., & Kordy, H. (2005). Construction, scoring and validation of the Short Evaluation of Eating Disorders (SEED). *European Eating Disorders Review, 13,* 191-200.

Baumeister, H., Reichler, L., Munzinger, M., & Lin, J. (2015). The impact of guidance on Internet-based mental health interventions: A systematic review. *Internet Interventions*, *1*, 205-215.

Beintner, I., Jacobi, C., & Taylor, C. B. (2011). Effects of an internet-based prevention programme for eating disorders in the USA and Germany: A meta-analytic review. *European Eating Disorders Review*, 20, 1-8.

Berg, K. C., Peterson, C. B., Frazier, P., & Crow, S. J. (2011). Psychometric evaluation of the Eating Disorder Examination and Eating Disorder Examination-Questionnaire: A systematic review of the literature. *Int J Eat Disord*, *45*, 428-438.

Berkman, N. D. L. (2007). Outcomes of eating disorders: A systematic review of the literature. International Journal of Eating Disorders, 40, 293-309.

Bewell, C. V. & Carter, J. C. (2008). Readiness to change mediates the impact of eating disorder symptomatology on treatment outcome in anorexia nervosa. *International Journal of Eating Disorders*, 41, 368-371.

Boudreaux, E. D., Sullivan, A., Abar, B., Bernstein, S. L., Ginde, A. A., & Camargo, C. A., Jr. (2012). Motivation rulers for smoking cessation: a prospective observational examination of construct and predictive validity. *Addict.Sci Clin Pract*, *7*, 8.

Carrard, I., Fernández-Aranda, F., Lam, T., Nevonen, L., Liwowsky, I., Volkart, A. C., Rouget, P., Golay, A., Van der Linden, M., & Norring, C. (2011). Evaluation of a guided Internet self-treatment programme for bulimia nervosa in several European countries. *European Eating Disorders Review*, 19, 138-149.

Dingemans, A. E., Danner, U. N., Donker, J. M., Aardoom, J. J., van, M. F., Tobias, K., van Elburg, A. A., & van Furth, E. F. (2014). The effectiveness of cognitive remediation therapy in patients with a severe or enduring eating disorder: a randomized controlled trial. *Psychother Psychosom, 83,* 29-36.

Dingemans, A.E., van Son, G.E., Aardoom, J.J., Bruidegom, K., Slof-Op 't Landt, M.C.T., & van Furth, E.F. (2016). Predictors of psychological outcome in patients with eating disorders: A routine outcome monitoring study. *International Journal of Eating Disorders, In press*.

Doove, L. L., Dusseldorp, E., van Deun, K., & van Mechelen, I. (2014). A comparison of five recursive partitioning methods to find person subgroups involved in meaningful treatment–subgroup interactions. *Advances in Data Analysis and Classification*, *8*, 403-425.

Ehring, T., Raes, F., Weidacker, K., & Emmelkamp, P. M. G. (2012). Validation of the Dutch Version of the Perseverative Thinking Questionnaire (PTQ-NL). *European Journal of Psychological Assessment*, 28, 102-108.

Fairburn, C. G. & Beglin, S. J. (2008). Eating Disorder Examination Questionnaire (EDE-Q 6.0).

In C.G.Fairburn (Ed.), Cognitive behavior therapy and eating disorders (pp. 309-313). New York:

Guilford Press.

Fernández-Aranda, F., Nunez, A., Martinez, C., Krug, I., Cappozzo, M., Carrard, I., Rouget, P., Jimenez-Murcia, S., Granero, R., Penelo, E., Santamaria, J., & Lam, T. (2009). Internet-based

cognitive-behavioral therapy for bulimia nervosa: A controlled study. *Cyberpsychology & Behavior,* 12, 37-41.

Fichter, M. M., Quadflieg, N., & Hedlund, S. (2006). Twelve-year course and outcome predictors of anorexia nervosa. *International Journal of Eating Disorders*, *39*, 87-100.

Fichter, M. M., Quadflieg, N., & Hedlund, S. (2008). Long-term course of binge eating disorder and bulimia nervosa: Relevance for nosology and diagnostic criteria. *International Journal of Eating Disorders*, *41*, 577-586.

Fokkema, M., Smits, N., Kelderman, H., & Penninx, B. W. (2015). Connecting clinical and actuarial prediction with rule-based methods. *Psychol Assess*, *27*, 636-644.

Frazier, P. A., Tix, A. P., & Barron, K. E. (2004). Testing moderator and mediator effects in counseling psychology research. *Journal of Counseling Psychology*, *51*, 115-134.

Genders, R. & Tchanturia, K. (2010). Cognitive remediation therapy (CRT) for anorexia in group format: A pilot study. *Eating and Weight Disorders*, *15*, e234-e239.

Grilo, C. M., Masheb, R. M., & Crosby, R. D. (2012). Predictors and moderators of response to cognitive behavioral therapy and medication for the treatment of binge eating disorder. *Journal of Consulting and Clinical Psychology*, *80*, 897-906.

Hilbert, A. & Tuschen-Caffier, B. (2007). Maintenance of binge eating through negative mood: a naturalistic comparison of binge eating disorder and bulimia nervosa. *International Journal of Eating Disorders*, 40, 521-530.

Hogdahl, L., Birgegard, A., & Bjorck, C. (2013). How effective is bibliotherapy-based self-help cognitive behavioral therapy with Internet support in clinical settings? Results from a pilot study. *Eating and Weight Disorders*, 18, 37-44.

Hothorn, T. & Zeileis, A. (2015). partykit: A modular toolkit for recursive partytioning in R.

Jacobi, C., Fittig, E., Bryson, S. W., Wilfley, D., Kraemer, H. C., & Taylor, C. B. (2011). Who is really at risk? Identifying risk factors for subthreshold and full syndrome eating disorders in a high-risk sample. *Psychological Medicine*, *41*, 1939-1949.

Jacobi, C., Völker, U., Trockel, M. T., & Taylor, C. B. (2011). Effects of an Internet-based intervention for subthreshold eating disorders: A randomized controlled trial. *Behaviour Research And Therapy*.

Keel, P. K. & Brown, T. A. (2010). Update on course and outcome in eating disorders. *International Journal of Eating Disorders*, 43, 195-204.

Kelders, S. M., Bohlmeijer, E. T., Pots, W. T., & van Gemert-Pijnen, J. E. (2015). Comparing human and automated support for depression: Fractional factorial randomized controlled trial.

Behaviour Research And Therapy, 72, 72-80.

Kraemer, H. C., Wilson, G. T., Fairburn, C. G., & Agras, W. S. (2002). Mediators and moderators of treatment effects in randomized clinical trials. *Archives of General Psychiatry*, *59*, 877-883.

Kroenke, K., Spitzer, R. L., Williams, J. B. W., & Löwe, B. (2009). An ultra-brief screening scale for anxiety and depression: The PHQ–4. *Psychosomatics*, *50*, 613-621.

Ljotsson, B., Lundin, C., Mitsell, K., Carlbring, P., Ramklint, M., & Ghaderi, A. (2007). Remote treatment of bulimia nervosa and binge eating disorder: A randomized trial of Internet-assisted cognitive behavioural therapy. *Behaviour Research And Therapy*, 45, 649-661.

Martignon, L., Vitouch, O., Takezawa, M., & Forster, M. (2003). Naive and yet enlightened: From natural frequencies to fast and frugal decision trees. In Wiley (Ed.), <u>Thinking: Psychological perspective on reasoning, judgement, and decision making</u> (pp. 189-211). West Sussex, England.

Melioli, T., Bauer, S., Franko, D. L., Moessner, M., Ozer, F., Chabrol, H., & Rodgers, R. F. (2016). Reducing eating disorder symptoms and risk factors using the internet: A meta-analytic review. *International Journal of Eating Disorders*, 49, 19-31.

National Institute for Clinical Excellence (2004). *Eating disorders: Core interventions in the treatment and management of Anorexia Nervosa, Bulimia Nervosa, and related eating disorders.*London.

R Development Core Team (2014). R: A language and environment for statistical computing [Computer software]. R Foundation for Statistical Computing, Vienna, Austria.

Schmidt, U. & Treasure, J. (2006). Anorexia nervosa: valued and visible. A cognitive-interpersonal maintenance model and its implications for research and practice. *British Journal of Clinical Psychology*, 45, 343-366.

Spek, V., Cuijpers, P., Nyklícek, N., Riper, H., Keyzer, J., & Pop, V. (2007). Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: A meta-analysis. *Psychological Medicine*, *37*, 319-328.

Steele, A. L., Bergin, J., & Wade, T. D. (2011). Self-efficacy as a robust predictor of outcome in guided self-help treatment for broadly defined bulimia nervosa. *International Journal of Eating Disorders*, 44, 389-396.

Stice, E., Marti, C. N., & Durant, S. (2011). Risk factors for onset of eating disorders: evidence of multiple risk pathways from an 8-year prospective study. *Behaviour Research And Therapy, 49,* 622-627.

Stice, E., Rohde, P., Shaw, H., & Marti, C. N. (2012). Efficacy trial of a selective prevention program targeting both eating disorder symptoms and unhealthy weight gain among female college students. *Journal of Consulting and Clinical Psychology*, 80, 164-170.

Stice, E., Rohde, P., Shaw, H., & Marti, C. N. (2013). Efficacy trial of a selective prevention program targeting both eating disorders and obesity among female college students: 1- and 2-year follow-up effects. *Journal of Consulting and Clinical Psychology, 81*, 183-189.

Stice, E., Marti, C. N., Spoor, S., Presnell, K., & Shaw, H. (2008). Dissonance and healthy weight eating disorder prevention programs: Long-term effects from a randomized efficacy trial. *Journal of Consulting and Clinical Psychology, 76,* 329-340.

Stice, E., Marti, N., Shaw, H., & O'Neil, K. (2008). General and program-specific moderators of two eating disorder prevention programs. *International Journal of Eating Disorders*, 41, 611-617.

Taylor, C. B., Bryson, S., Luce, K. H., Cunning, D., Doyle, A. C., Abascal, L. B., Rockwell, R., Dev, P., Winzelberg, A. J., & Wilfley, D. E. (2006). Prevention of eating disorders in at-risk college-age women. *Archives of General Psychiatry*, *63*, 881-888.

Volker, U., Jacobi, C., Trockel, M. T., & Taylor, C. B. (2014). Moderators and mediators of outcome in Internet-based indicated prevention for eating disorders. *Behaviour Research And Therapy, 63C,* 114-121.

Wade, T. D., Frayne, A., Edwards, S. A., Robertson, T., & Gilchrist, P. (2009). Motivational change in an inpatient anorexia nervosa population and implications for treatment. *Australian and New Zealand Journal of Psychiatry*, *43*, 235-243.

Wagner, G., Penelo, E., Nobis, G., Mayrhofer, A., Wanner, C., Schau, J., Spitzer, M., Gwinner, P., Trofaier, M. L., Imgart, H., Fernandez-Aranda, F., & Karwautz, A. (2015). Predictors for good

therapeutic outcome and drop-out in technology assisted guided self-help in the treatment of bulimia nervosa and bulimia like phenotype. *European Eating Disorders Review, 23,* 163-169.

Wagner, G., Penelo, E., Wanner, C., Gwinner, P., Trofaier, M. L., Imgart, H., Waldherr, K., Wober-Bingol, C., & Karwautz, A. F. (2013). Internet-delivered cognitive-behavioural therapy v. conventional guided self-help for bulimia nervosa: Long-term evaluation of a randomised controlled trial. *Br J Psychiatry*, 202.

Warmerdam, L., van, S. A., Jongsma, J., Twisk, J., & Cuijpers, P. (2010). Online cognitive behavioral therapy and problem-solving therapy for depressive symptoms: Exploring mechanisms of change. *J Behav Ther Exp.Psychiatry*, 41, 64-70.

Weiss, C. V., Mills, J. S., Westra, H. A., & Carter, J. C. (2013). A preliminary study of motivational interviewing as a prelude to intensive treatment for an eating disorder. *J Eat Disord, 1,* 34.

Wilson, G. T., Grilo, C. M., & Vitousek, K. M. (2007). Psychological treatment of eating disorders. *American Psychologist*, *62*, 199-216.

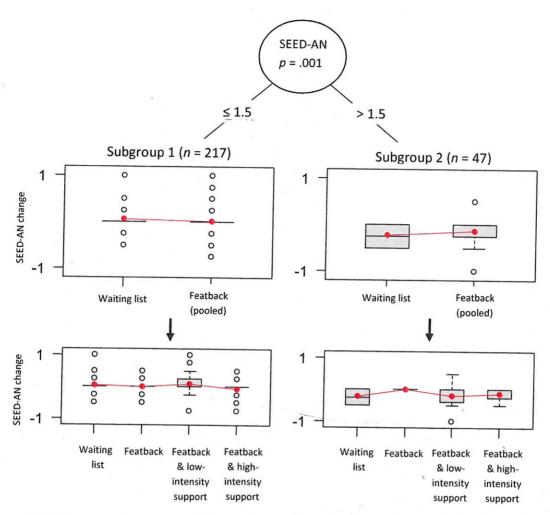
Wilson, G. T., Wilfley, D. E., Agras, W. S., & Bryson, S. W. (2010). Psychological treatments of binge eating disorder. *Archives of General Psychiatry*, *67*, 94-101.

Wolk, S. L. & Devlin, M. J. (2001). Stage of change as a predictor of response to psychotherapy for bulimia nervosa. *International Journal of Eating Disorders*, *30*, 96-100.

Zeileis, A., Hothorn, T., & Hornik, K. (2008). Model-based recursive partitioning. *Journal of Computational and GraphicalStatistics*, *17*, 492-514.

Zeileis, A., 2015. A Unified Approach to Structural Change Tests Based on ML Scores, *F* Statistics, and OLS Residuals. *Econometric Reviews*, *24*(4), 445–466

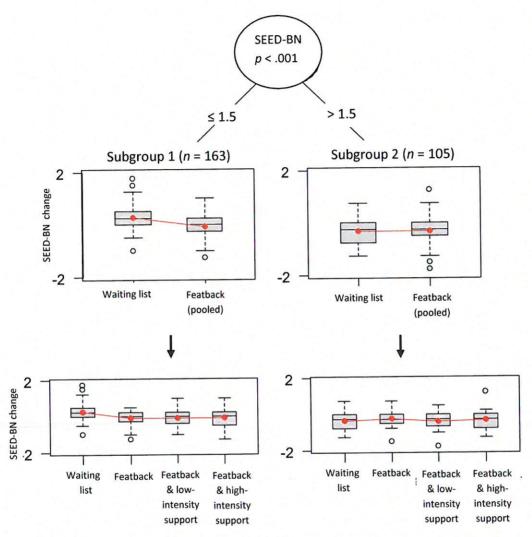
Figure 1. The results of a model-based recursive partitioning analysis with change in anorectic psychopathology (post-intervention minus baseline) as outcome measure.



SEED-AN = Anorectic psychopathology as assessed by the Short Evaluation of Eating Disorders; Featback = an Internet-based intervention that was provided with three different levels of therapist support: none, low-intensity (once a week), and high-intensity (three times a week).

Note: Lower SEED-AN change scores represent greater reductions in anorectic psychopathology

Figure 2. The results of a model-based recursive partitioning analysis with change in bulimic psychopathology (post-intervention minus baseline) as outcome measure.



SEED-BN = Bulimic psychopathology as assessed by the Short Evaluation of Eating Disorders; Featback = an Internet-based intervention that was provided with three different levels of therapist support: none, low-intensity (once a week), and high-intensity (three times a week).

Note: Lower SEED-BN change scores represent greater reductions in bulimic psychopathology