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Early response to psychological treatment for eating disorders: A systematic review and meta-analysis

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The authors declare they have no conflict of interest.

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Abstract

Early response is a well-established predictor of positive outcomes at the end of psychological treatments for common mental disorders. There is some prior evidence that this conclusion also applies to eating disorders, including three meta-analyses, but no moderators of that relationship have been identified. However, a number of further papers have been published since, which might influence the size of the effect of early response or the potential role of moderating factors. This pre-registered systematic review presents a comprehensive examination of this literature. Three databases were searched (Scopus, PsycInfo, PubMed). In total, 33 eligible studies were included in a narrative synthesis, and 25 studies were included in random-effects meta-analysis. The majority (91%) of studies were rated as having low or moderate risk of bias. Approximately half of patients across clinical samples showed early response to psychological therapy, which was most often defined as reliable symptomatic improvement during the first four sessions. A significant and moderate association was found between early response and post-treatment outcomes (r = 0.41 [95% CI: 0.32-0.481], p < .0001). Significant evidence of heterogeneity (Q[28] = 136.42, p < .0001; I^2 = 80.2%) was evident. The review was limited by the exclusion of grey literature and only 76% of studies provided sufficient statistical information for meta-analytic synthesis, although we found no significant evidence of publication bias, $\chi^2(1) = 0.001$, p = .97. Overall, evidence accumulated over twenty years establishes early response as the most robust predictor of treatment outcomes in the field of eating disorders. However, only half of patients show early change in this way. Further research is needed to determine whether there are patient or clinician characteristics that predict early response to psychological treatment for eating disorders.

Key words: Eating disorders; psychological therapies; early response; outcomes; meta-analysis

Early Response to Psychological Treatment for Eating Disorders:

A Systematic Review and Meta-analysis

Eating disorders are characterised by overvaluation of shape/weight and abnormal eating behaviors, including severe restriction of food intake, frequent use of binge-eating, and/or purging behaviours (Jansen, 2016). They can cause impairments to the physical and mental health of the affected individual (American Psychological Association, 2013). The lifetime prevalence of eating disorders is roughly 5% - 0.6% for AN, 1% for BN, and 3% for BED (Treasure, Claudino & Zucker, 2010). They are most likely to develop in adolescence (Steinhausen, Gavez & Winkler Metzke, 2005), and are more prevalent among females than males (Striegel-Moore, Rosselli, Perrin, DeBar, Wilson, May & Kraemer, 2009). There are several sub-types – most prominently, anorexia nervosa, bulimia nervosa, binge-eating disorder, other specified feeding and eating disorder (OSFED) and avoidant/restrictive food intake disorder (ARFID), as well as less common diagnoses such as unspecified feeding or rating disorder, pica and rumination disorder (National Institute of Mental Health, 2016). These disorders are commonly comorbid with anxiety-based disorders, depression, and personality pathology (e.g., Jordan, Joyce, Horn, McIntosh, Luty, McKenzie, Frampton, Mulder & Bulik, 2008; Swinbourne, Hunt, Abbott, Russell, St Clare & Touyz, 2012).

If they are not treated successfully, eating disorders can be disabling and chronic mental disorders (Klump, Bulik, Kaye, Treasure & Tyson, 2009), with serious impact on the individual's quality of life and that of their carers (e.g., Le, Mihalopoulos, Engel, Touyz, González-Chica, Stocks & Hay, 2019). Treatments need to be able to produce clinically meaningful benefits in terms of eating attitudes and behaviors, biological change, and wider emotional, social and cognitive change. The current evidence base (e.g., National Institute for Health and Clinical Evidence [NICE], 2017) indicates that there are a number of effective psychological treatments for eating disorders, such as cognitive behavioral therapy, family-based treatment, and specialist supportive clinical management. Other psychological therapies also have some preliminary evidence (e.g., interpersonal psychotherapy – Hilbert, Hildebrandt, Agras, Wilfley & Wilson, 2015; dialectical behavioral therapy - Safer & Joyce,

2011). In contrast, pharmacological interventions are not recommended as first line treatments according to current clinical guidelines (NICE, 2017).

The goal of treatments for eating disorders needs to include the prevention of relapse, which is dependent on the initial achievement of remission. Therefore, it is important that treatment should address potential relapse risk factors, including residual pathological eating behaviours and attitudes, remaining underweight at the end of treatment, and pathological levels of negative body image. Treatment-dose effects are not linear in eating disorders, meaning that additional treatment sessions do not yield as much improvement as the early ones, with most symptomatic improvement occurring over the first eight sessions (e.g., Bell, Waller, Shafran & Delgadillo, 2017). Therefore, achieving stable remission and recovery depends largely on changes that occur early in treatment for eating disorders. This pattern fits with wider evidence that early response, usually defined as statistically significant symptomatic reductions during the first four sessions of therapy, is a well-established and replicated predictor of psychological treatment outcomes for depression and anxiety disorders (Beard & Delgadillo, 2019).

The importance of early response in the field of eating disorders was initially highlighted by Vall and Wade (2015), who conducted a broad review of predictors of eating disorder treatment outcomes. Linardon, Brennan and de la Piedad Garcia (2016) reached a similar overall conclusion in a meta-analysis based on similar but more targeted literature reviewed approximately a year later, though their overall effect sizes (behavioural outcomes – $r = 0.397$; cognitive outcomes – $r = 0.288$) were smaller than those of Vall and Wade (2015). However, while Vall and Wade (2015 - Table 2) identified 12 relevant studies for their meta-analysis, the broad scope of their study meant that their search strategy was not specifically devised to be sensitive and specific to early response studies (i.e., their wider aim was to identify a much wider range of predictors of outcome). Consequently, several of the 20 studies that were identified by Linardon et al. (2016 – Table 1) overlapped the period of time that Vall and Wade considered, but were not represented in the earlier review. A further meta-analysis (Nazar, Gregor, Albano, Marchica, Coco, Cardi & Treasure, 2017) has considered the role of

early change in predicting subsequent diagnostic change, but identified fewer papers (*N* = 14) than Linardon et al. (2016), due to the more constrained eligibility criteria for inclusion (diagnostic outcomes). Given that several years have elapsed since the previous analyses and several studies on the impact of early change in eating disorders have emerged since the Vall and Wade (2015) and Linardon et al. (2016) meta-analyses (e.g., Bell et al., 2017; Hilbert, Herpertz, Zipfel, Tuschen-Caffier, Friederich, Mayr, Crosby & de Zwaan, 2019; Matheson, Gorrell, Bohon, Agras, Le Grange & Lock, 2020), it is important to revisit this topic to determine whether the impact of early change confirms the reduction in effect sizes between the Vall and Wade (2015) and Linardon et al. (2016) studies.

While Linardon et al. (2016) did not find any evidence of moderators of the impact of early change, these new studies require reconsideration of that conclusion. Studies vary in their definitions of the time frame of early change, with some defining it as within the first month of treatment, and others defining early change as early as one week or as late as 10 weeks (e.g., Hilbert et al., 2019; Lock, Couturier, Bryson & Agras, 2006; MacDonald, McFarlane, Dionne, David & Olmsted, 2017). Furthermore, studies vary in their definition of 'early change', with categorical definitions that include a fixed level of change (e.g., a reduction of binges by 65% - Masheb & Grilo, 2007), and dimensional levels of change where greater early change is associated with later outcomes. Finally, it is not clear whether the impact of early change is limited to well-controlled efficacy-based research studies, or whether it applies to effectiveness studies, carried out in routine clinical settings. Therefore, addressing the core research question here also depends on understanding potential factors that might moderate the overall effect of early change in psychotherapy for eating disorders.

The present systematic review and meta-analysis aimed to provide a comprehensive qualitative and quantitative synthesis of the contemporary literature on the early response phenomenon in the psychological treatment of eating disorders. The following research questions guided this review:

1. Is early response to psychological treatment significantly associated with post-treatment outcomes?

2. At which session of therapy is early response usually defined?
3. Does the relationship between early change and treatment outcome differ in efficacy versus effectiveness studies?
4. Do the findings of contemporary studies differ compared to those of the earlier systematic review by Vall and Wade (2015)?

Method

Protocol registration

The protocol for this systematic review was pre-registered in the PROSPERO database (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=180039).

Search strategy and study selection

The inclusion and exclusion criteria that guided this review are listed in Table 1. Searches were performed across three databases (SCOPUS, PSYCinfo and PubMed) on April 25, 2020, using variations of the following search terms:

1. Anorexia OR bulimia OR binge eating disorder OR eating disorder; AND
2. Early OR rapid OR sudden ADJ gain* OR response OR symptom* OR improvement* OR change*; AND
3. Therap* OR treatment* OR intervention* OR support; AND
4. Outcome

The search was limited to peer-reviewed scientific journal articles published in English. No date restrictions were applied. The grey literature was not searched, in keeping with the pre-registration plans on PROSPERO, to ensure that the research reported used met the criterion of being successfully peer-reviewed. The specific search strategies used for each database are included in Supplementary Material A. Reverse citations and reference lists of eligible studies were hand-searched to identify further potentially eligible studies. Note that the plural term ‘eating disorders’ was not used, though none of the searches (under other diagnostic terms, for reverse citations, or of reference lists of eligible papers) identified any new papers that used that term. Figure 1 shows a PRISMA diagram, summarising the study selection process. Study selection and extraction were performed by the first author, and queries about

suitability were resolved in consultation with the other co-authors. Details of the 10 excluded studies are provided in Supplementary Material B, along with reasons for exclusion.

***Table 1**: Study Inclusion and Exclusion Criteria*

	Inclusion Criteria	Exclusion Criteria
Population	• Participants who have an eating disorder diagnosis and have received psychological treatment for their eating disorder. • Participants must be aged 12 or older.	• Participants who have not received psychological treatment for their condition. • Participants under the age of 12.
Intervention	• Any psychological intervention used to treat eating disorders, in any modality (individual, group, online etc.)	• Studies that include eating disorder treatments that do not involve a psychological component.
Comparator	• Between-group comparisons of rapid vs. non-rapid responders. • Studies that examine early response as a predictor of outcome in eating disorder treatments. Early response was defined and coded either dimensionally (e.g., level of change over a specified number of early sessions) or categorically (e.g., reliable or clinically significant change over those early sessions)	• Studies that do not examine early response as a predictor of treatment outcome.
Outcome	• The statistical significance and magnitude of the association between early response to eating disorder treatment and outcomes.	• Studies where early response is not measured. • Studies where post-treatment outcomes of eating disorder treatment are not measured.
Setting	• Any settings which psychological interventions are usually delivered to treat eating disorders.	
Study Design	• Randomised control trials and observational studies. • Studies published in peer-reviewed scientific journals.	• Grey literature (e.g. dissertations), studies not published in peer-reviewed scientific journals, quasi-experimental designs. • Studies not published in English.

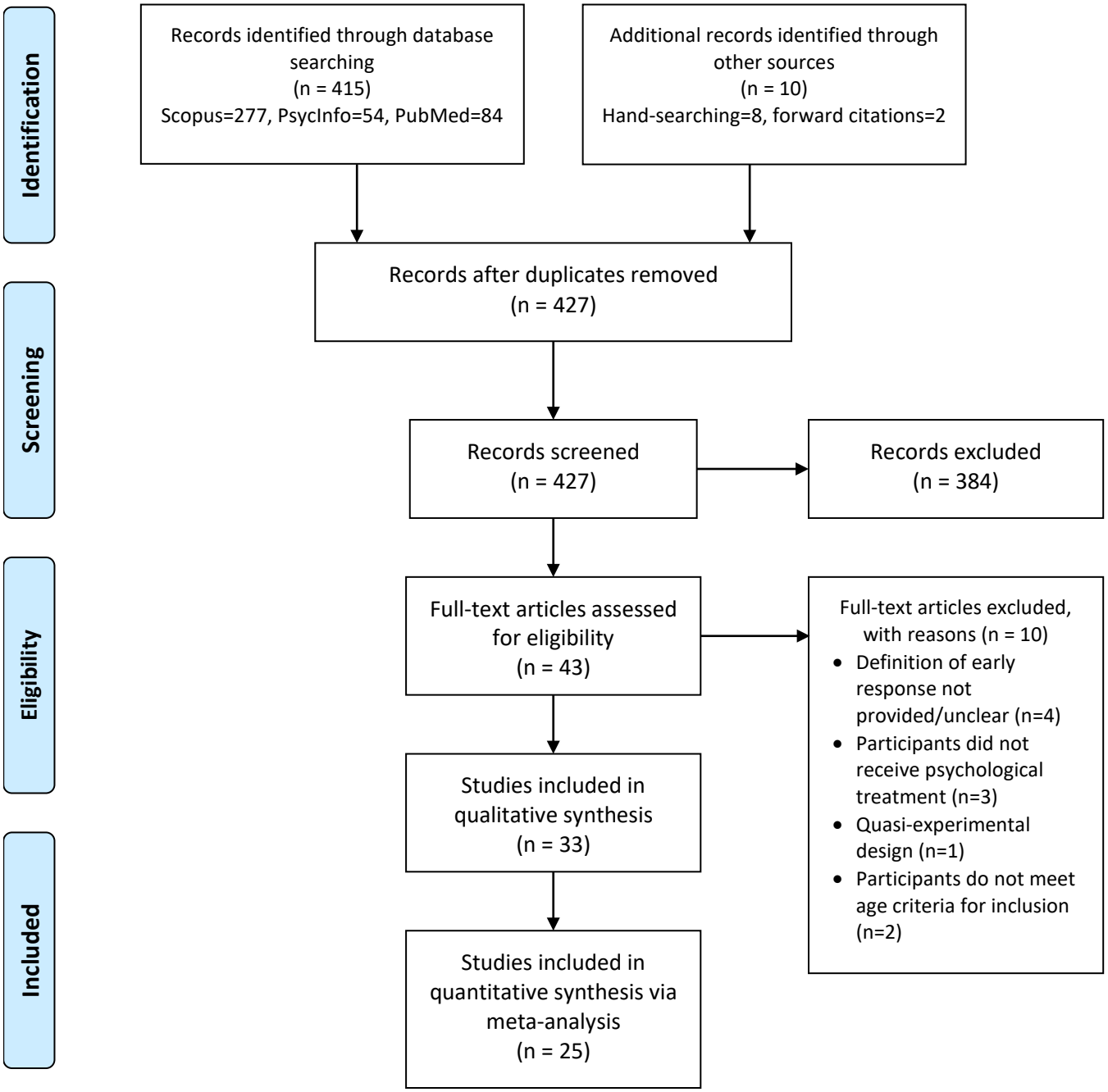

Figure 1: PRISMA Flow Diagram Demonstrating the Study Selection.

Risk of Bias Assessments

Two authors independently assessed the risk of bias (RoB) for each study. The Revised Cochrane Risk of Bias Tool for Randomized Trials (RoB 2) (Cochrane Methods,

2020) was used to assess risk of bias in randomised control trials, and Critical Appraisal Skills (CASP) checklist was used for cohort studies (CASP, 2017). RoB ratings were highly consistent and did not require mediation by a third reviewer (kappa = 0.82). Summary tables for risk of bias ratings can be found in Supplementary Materials C and D.

Data Analysis

In addition to a narrative synthesis of all studies included in the review, a random-effects meta-analysis was conducted using the statistical package Meta-Analysis via Shiny (MAVIS; Hamilton, 2011). Studies that examined early response as a predictor of psychotherapy treatment outcomes that provided sufficient statistical information to calculate a single *r* correlation coefficient were included in the meta-analysis. In studies that provided an effect size (Cohen's *d*), this statistic was converted to an *r* value using an effect size converter (DeCoster, 2012; Lenhard & Lenhard, 2016) to ensure the same test statistic was used across all studies. Studies that did not include post-treatment outcome data, studies that did not provide sufficient statistical data and whose corresponding authors did not respond to data requests were excluded from the meta-analysis. Overall, twenty-six studies were included in the meta-analysis.

The primary meta-analysis examined within-group effects of early response by calculating a pooled correlation co-efficient for all studies. Heterogeneity was examined using Cochrane's Q and I^2 statistics (Higgins, Thompson, Deeks & Altman, 2003). Publication bias was examined using a weight function model (Vevea & Hedges, 1995) and funnel plots (Egger & Smith, 1997).

There were several sources of heterogeneity in the design of the studies, including the eating disorder being studied, the symptom measures used, the time-point at which early response was defined, the use of categorical (e.g., a fixed percentage reduction in outcome measures) vs. dimensional (level of change in the target outcome measure) definitions of early response, and the time-point at which outcomes were assessed (e.g., end-of-treatment, 6-month follow up). In studies with multiple similar outcome measures (e.g., different sub-scales of the EDE-Q), a pooled correlation co-efficient was calculated.

In studies that investigated multiple distinctive outcomes (e.g., EDE-Q and BMI) in the same sample, the outcome measure that explained the most variance within the cohort was used. Consistent with prior research (e.g., Beard & Delgadillo, 2019), the measurement point closest to Session 4 was used in studies that examined early response at multiple time points, with outcomes defined at the end of treatment. Study authors were emailed to request missing data to maximise the completeness of meta-analytic review. Sources of heterogeneity, such as difference in study design, treatment modality, primary diagnosis in the sample, differences in primary outcome measure, measurement approach (categorical vs. dimensional), and risk of bias classification were examined using categorical moderator analyses.

Results

Narrative synthesis

Design and sample characteristics

Thirty-four studies met the inclusion criteria and are described in Tables 2 (characteristics) and 3 (outcomes). Of the included studies, thirteen were RCTs and twenty-one were cohort studies. Studies investigated a range of eating disorders, including bulimia nervosa (n = 9), binge-eating disorder (n = 7) and anorexia nervosa (n = 5). Eleven of the 34 included studies included “mixed” samples with a range of eating disorder diagnoses. Sample sizes ranged from 42 to 241, with a total of 3,552 participants across all studies. Nearly all studies had predominantly female samples, with five having all-female samples.

Measures of early response

As shown in Table 2, a range of measures were used to quantify early response. The EDE, either in interview (EDE-I) or questionnaire format (EDE-Q), was commonly used to measure eating disorder pathology. Body Mass Index (BMI) measurements and changes in weight were also commonly used as measures of early response in studies where early response was defined by changes in weight. In studies where early response was defined by a reduction in episodes of binging and/or purging behaviours, self-report measures of binge/purge habit frequency (e.g., objective binge episode (OBE) measures), were sometimes used alongside the EDE.

Interventions

Almost all of the included studies focused solely on psychological interventions (n = 31), with CBT being the most commonly studied treatment modality (n = 18). Other treatment modalities investigated in included studies included family-based therapy (FBT), interpersonal psychotherapy (IPT), psychoeducation, dialectical behaviour therapy (DBT), behavioural weight loss (BWL), compassion-focused therapy (CFT), adolescent-focused therapy (AFT), active comparison group therapy (ACGT), individual-supported therapy, supportive psychotherapy (SPT), guided self-help and motivational interviewing (MI). Four studies used treatments that combined elements from multiple treatment modalities. Of the remaining three studies, one used a combination of CBT with either a drug or placebo (Grilo & Masheb, 2007), and the other one combined psychological interventions with a dietary intervention (Wales, Brewin, Cashmore, Haycraft, Baggott, Cooper & Arcelus, 2016).

Risk of bias assessment

Of the studies reviewed, half were found to have a “moderate” risk of bias (n = 17). Fourteen had a “low” risk of bias, and the remainder had a “high” risk of bias (n = 3). The most common reasons for a study being rated as having a risk of bias included lack of follow-up with regards to missing data, failure to explain participant dropouts, failure to control for baseline characteristics or confounding variables, and use of self-report measures for treatment outcomes.

Is early response to treatment significantly associated with outcome?

Based on available data across included studies, over half (54.4%) of study participants were classed as early responders. The majority of these studies (n = 31) found significant differences in end-of-treatment outcome between early and non-early responders, with early responders more likely to remit from their disorder. Early response was associated with positive treatment outcomes across a range of eating disorder types (anorexia nervosa, bulimia nervosa, binge eating disorder), and in studies that included mixed samples (participants with different ED diagnoses). Early response was also associated with positive treatment outcomes across different outcome measures (EDE-Q, EDE-I, objective binge

episodes and weight-based measures). Two studies compared rates of early response across psychotherapy modalities (Hilbert et al., 2015; MacDonald et al., 2017). Both found greater rates of remission in CBT conditions compared to non-CBT conditions.

Of the included studies, only two did not report early response as a significant predictor of treatment outcome (Fernandez-Aranda, Alvarez-Moya, Martínez-Viana, Sanchez, Granero, Penelo, et al. 2009; Raykos, McEvoy, Erceg-Hurn, Byrne, Fursland & Nathan, 2014). Fernandez-Aranda et al. primarily focused on predictors of early response in bulimia nervosa, and found that presence of binge-purge habits at treatment session 4 was a significant predictor of poor early response. However, this study did not identify any significant predictors of end-of-treatment outcome. Rakyos et al. examined the role of early therapeutic alliance on treatment outcome for CBT in bulimia nervosa and found no significant effects of early therapeutic alliance on treatment outcome.

Some of the reviewed studies did not specifically test early response–outcome associations. Instead, they focused on when the largest changes occurred, or at which session early changes predicted end-of-treatment outcome (Doyle, Le Grange, Loeb, Doyle & Crosby, 2010; Le Grange et al, 2014; Le Grange, Accurso, Lock, Agras & Bryson, 2006; Marrone, Mitchell, Crosby, Wonderlich & Jollie-Trottier, 2009; Matheson et al., 2020; Zunker, Peterson, Cao, Mitchell, Wonderlich, Crow & Crosby, 2010).

Furthermore, some of the reviewed studies used multiple definitions of early response and compared rates of remission at end-of-treatment across definitions (Hilbert et al., 2019; MacDonald et al., 2015). Hilbert et al. found significantly higher rates of remission from binge-eating disorder in early responders who met early response criteria at week 1 (reduction in binge-eating of 10% or greater) when compared to non-early responders, but did not find a significant difference between early and non-early responders based on early response criteria for week 4 (reduction in binge-eating of 70% or greater). MacDonald et al. used both percentage and frequency-based definitions for early response at weeks 2 and 4 of treatment for binge-purge habits in bulimia nervosa and purging disorder patients, finding significant differences in end-of-treatment binge-purge frequencies across all four definitions, with early

responders having significantly fewer binge-purge episodes than non-early responders. However, the only definition that remained significant at follow-up assessment was 'three or fewer binge-purge episodes in the first four weeks of treatment'.

At which session is early response usually defined?

As shown in Table 3, there was variety in the time at which early response was measured. Twenty-two of the thirty-four studies (65%) conceptualised early response by quantifying early change between intake assessment and the fourth week of treatment. Other studies conceptualised this as early as the first week of treatment, or as late as the tenth. Twelve studies provided categorical definitions of early response (e.g. a reduction of 70% in the target symptom from baseline to the week of early response), or a pre-defined, quantitative reduction in eating-disorder related behaviours (e.g., three or fewer binge-eating episodes over the first four weeks of treatment). Remaining studies investigated early response as a dimensional measure, examining the effects of early change magnitude on early response (i.e. do higher levels of early change predict better treatment outcome?). With regards to the relationship between early response and outcomes, a range of data analysis methods were used, including Receiver Operating Characteristic Curves (ROC), multiple regression, logistic regression, general linear models (GLMs), mixed-model analyses and multi-level modelling (MLM).

Table 2. Key characteristics of included studies.

FIRST AUTHOR & YEAR	*STUDY DESIGN*	*STUDY SETTING*	*ED SUBTYPE(S)*	*N*	*ANALYSED N*	*INTERVENTION CONDITION*	*OUTCOME MEASURE*	*INTERVENTION DURATION*	*ANALYSIS*	*AGE*
Agras et al. (2000)	Cohort study	Patients receiving treatments at one of three treatment sites	Bulimia Nervosa (BN)	194	188	CBT	EDE Interview (EDE-I)	18 sessions over 16 weeks	Chi-square – comparing dropouts vs completers.	Mean age = 28.1 (all female ppts)
Bell et al. (2017)	Cohort study (secondary data analysis)	Participant data taken from an eating disorder treatment centre (UK)	BN, Binge-eating disorder (BED), Anorexia Nervosa (AN)	164	164	Various psychotherapy models	BMI, EDE-Q	Up to 18 months	Effect sizes for clinical outcomes, MANOVA for treatment outcomes, partial correlations	Mean: 30.13
Doyle et al. (2010)	Cohort Study	Participants had previously been hospitalised for weight restoration	AN	65	65	FBT	Ideal Body Weight (IBW)	20 sessions	Receiver Operator Characteristics (ROC) – Area Under Curve (AUC)	Mean age: 14.9 (SD = 2.1)
Fairburn (2004)	Cohort Study	Data taken from two treatment sites	BN	220	220	CBT/IPT	EDE. Purging frequency measured by computerised questionnaire	19 sessions over 20 weeks	Pearson's correlation (r)	Mean age= 28.1 (all female)
Fernandez-Aranda et al. (2009)	Cohort Study	Patients admitted to an ED unit at a University Hospital (Spain)	BN	241	241	Psychoeducational therapy	Food diary – assessed binge/purge habits	6 sessions	Logistic regression (abstinence from binge/purge), multiple regression (% reduction in binge/purge)	Range: 17-57

Grilo & Masheb (2007)	RCT	Yale Medical School (USA)	BED	50	50	Drug + CBTgsh vs placebo + CBTgsh	EDE-I (remission), weight loss	12 weeks	Intent-to-treat analysis (ITT)	Range: 35-60
Hartmann et al. (2007)	Cohort Study	Department of Psychosomatic Medicine & Psychotherapy, Freiburg (Germany)	AN	227	85	Psychodynamic, but treatment incorporates cognitive-behavioural elements	BMI, EDI	Treatment lasts until patients reach target weight – they then stay for 6-8 more weeks. Minumum 6 weeks of treatment.	Regression, AUC	17+
Hilbert et al. (2015)	RCT	Participants recruited from two treatment sites (Rutgers/Washington, USA)	BED	205	205	IPT vs CBTgsh vs BWL	EDE-I (psychopathology), self-reported OBE (binge habits)	BWL: 16 weekly sessions CBTgsh: 10 sessions: 4 weekly sessions, 2 2-weekly sessions, 4 4-weekly sessions IPT: 19 sessions: 3 sessions in 2 weeks, 12 weekly sessions, 4 2-weekly sessions	Binge: Kruskal-Wallis H. Chi-square & Cohen's delta used at followup. EDE: mixed linear model	18+
Hilbert et al. (2019)	Cohort study (Secondary data analysis)	Treatment sites in Germany/Switzerland	BED	86	83	CBT	OBE/EDE-Q	18 sessions over 4 months: 2/week for month 1, 1/week for months 2 and 3, 1 per 2 weeks for month 4	ROC (AUC)	18+
Kelly et al. (2014)	Cohort Study	Participants admitted to specialised day hospital treatment	AN(restricting) /AN(binge-purge)/BN/ not specified (EDNOS)	97	97	Compassion-Focused Therapy (CFT)	EDE-Q	12 weeks	Multi-level Modelling	Age range: 17-57

Keshen et al. (2017)	Cohort Study	Patients attending a group-based EDD program (Canada)	AN/AN(binge-purge subtype)/BN/ Unspecified ED	59	49	Group-based therapy that incorporates aspects of CBT, ACT, DBT	EDE-Q	4 days/week for up to 32 weeks	Hierarchical Regression	Age range: 18-53
Le Grange et al. (2008)	RCT	University of Chicago (USA)	BN	80	80	Family Therapy vs Individual Supportive Therapy	EDE-I	20 sessions	ROC (AUC)	Mean age = 16.1, (SD = 1.6)
Le Grange et al. (2014)	RCT – secondary data analysis	Two sites (Chicago/ Stanford, USA)	AN	121	121	FBT vs individual adolescent-focused therapy (AFT)	EDE-I, expected body weight	24h of therapy over a 12 month treatment period	ROC (AUC)	Mean age:= 14.4 (SD = 1.6)
Lock et al. (2006)	RCT – secondary data analysis	Hospital	AN	86	68	Family Therapy	EDE-I	EITHER 10 sessions + 6 months treatment, or 20 sessions + 12 months treatment	ANOVA/Chi-square + effect size (Cohen's d) + Area Under Curve (AUC)	Mean age: 15.1
MacDonald et al. (2015)	Cohort Study	Day hospital	BN/OSFED-PD	158	158	Day Hospital Program	EDE-I, EDE-Q, Self-report of binge/purge patterns	35-40 hrs per week for 6-8 weeks for a "full dose"	ROC – independent t-test used to compare outcome. Cohen's d reported for both 2/4wk categories	Age 17-57 (mean 27.1)
MacDonald et al. (2017)	RCT	Day Hospital	BN/purging disorder	44	44	CBT-RR + Day Hospital vs Motivational Interviewing (MI) + Day Hospital	EDE-Q, binge-purge frequency, Difficulties in Emotion	4 sessions of CBT/interviewing and then Day Hospital as normal	Intent-to-treat (ITT) – effect size (V/D) calculated. T-test for EoT outcomes	Mean: 27.3 (all female)

							Regulation Scale (DERS)			
MacDonald & Trottier (2019)	Cohort Study	Day hospital	BN/purging disorder	76	76	CBT	EDE-Q, CIA, Abstinence from binge-purge habits	>6 weeks	Logistic regression	Mean age: 29.7
Marrone et al. (2009)	RCT	Study conducted across nine areas in North Dakota/Minnesota (US).	BN	116	116	CBT – Telemedicine vs face-to-face	EDE-I	20 sessions over 16 weeks	ROC	18+
Masheb & Grilo (2007)	RCT	Participants used guided self help – guided by experienced doctoral research clinicians (Yale, USA)	BED	75	75	CBTgsh vs Behavioural Weight Loss (BWLgsh)	EDE-Q, Objective Binging Episodes (OBEs)	12 weeks, with 6 individual meetings	Mixed-model analysis (F-statistic obtained)	Range – 20-60
Matheson et al. (2020)	RCT (secondary data analysis)	Participants enrolled In a two-site treatment study	BN	71	71	CBT vs FBT vs SPT (supportive psychotherapy)	EDE-I	Varied – mean no. of sessions attended by sample was **13.6**	ROC	Aged 12-18
Munsch et al. (2012)	RCT	Patients recruited via newspaper advert/telephone interview – randomly allocated to one of two treatment conditions	BED – overweight to obese patients	80	52	CBT, Behavioural Weight-loss Treatment (BWL)	EDE-Q, BMI, self-reported binge eating episodes	16 treatment sessions	Linear regression	Range: 18-70
Olmsted et al. (1996)	Cohort Study	Patients receiving specialised day hospital treatment	BN	166	166	Group therapy	EDE-I (binge/purge)	Ranged from 4-18 weeks (average of 10.4 weeks)	Kruskall-Wallis ANOVA	Mean age: 25.3
Pellizzer	Cohort	Participants taken from	BN/OFSED/	62	62	CBT-T	EDE-Q, CIA	10 sessions	Linear regression	Range: 18-

et al. (2019)	Study	a treatment-seeking sample	UFED/BED, non-underweight							52
Raykos et al. (2013)	Cohort Study	Treated at a specialist public mental health service in Australia	Any eating disorder diagnosis	105	105	CBT-E	EDE-Q	20 sessions in 20 weeks (if not underweight), 40 sessions in 38 weeks (if underweight)	Chi-square (categorical), ANOVA (dimensional)	16+
Raykos et al. (2014)	Cohort Study	Treated at a specialist public mental health service in Australia	BN/atypical BN	112	112	CBT-E	EDE-Q	20 sessions ideal – varied in sample (mean 22.3, SD – 9.9)	Multiple regression	16+
Safer & Joyce (2011)	RCT	Sample taken from a previous study	BED	101	101	DBT vs ACGT	EDE-I	20 weeks	Chi-square (primary), Cohen's d (secondary)	18+
Thompson-Brenner et al. (2015)	RCT	Double-blind	BN	43	43	CBT-E	EDE-I, OBE	20 sessions (8 in first 4 weeks, then 12 in 16 weeks)	ROC	18-65 (female only)
Turner et al. (2015)	Cohort Study	Community ED service in the UK	AN/BN/ EDNOS	94	94	CBT	EDE-Q	Typically 20 sessions, but shortened to 10 in event of rapid response, and extended as far as 40 sessions in some cases	Linear regression	Range: 17-55

Turner et al. (2016)	Cohort Study	UK Treatment session (NHS)	AN/BN/ EDNOS	179	179	CBT	PBQ-SF, HADS (Hospital Anxiety & Depression scale)	Typically 20 sessions, but shortened to 10 in event of rapid response, and extended as far as 40 sessions in some cases.	Linear regression	Range: 17-53
Vaz et al. (2014)	Cohort Study	ED treatment centres in Portugal	BNEDNOS/ BED	42	42	Guided-Self Help	EDE-Q	8 sessions	Logistic regression	Mean = 26
Wales et al. (2016)	Cohort Study	Patients entering specialist inpatient treatment	AN	102	87	Diet, Group therapy (CBT/psychoeducation)	BMI	Varied – treatment lasts until patient reaches BMI of 17.5kg/m^2	Logistic Regression	18+
Waller et al. (2018)	Cohort Study – Case Series	Patients drawn from two NHS specialist clinics (UK)	EDNOS	106	64	CBT-T	EDE-Q	10 sessions	Multiple Regression	18+
Zunker et al. (2010)	RCT	Participants recruited from two US sites (North Dakota, Minnesota)	BED	185	179	CBT (therapist led, therapist assisted, self-help)	EDE	20 weeks	ROC	18+

Table 3. Outcomes reported by studies included in the review.

First Author & Year	RR Session	RR Definition – Categorical or Dimensional?	% of Early Responders	Between-Group Comparisons vs. Within-Group Effects	Outcomes
Agras et al. (2000)	Session 6 (week 4)	Dimensional – Reduction of purging behaviours	NA	Between-group comparisons – treatment responders vs. non-responders	Percentage change in purging by session 6 only significant predictor of outcome at end of treatment. (χ^2=42.5, df=1, p<0.001). Those who reduced purging by less than 70% were more likely to be treatment non-responders.
Bell et al. (2017)	Session 8	Categorical -EDE-Q change score of 1.13 or greater.	34.8% (EDE-Q global)	Within-group effects	Pre-post effect size (Cohen's d) of EDE-Q global score = 1.42. Rapid response in EDE-Q global scores predicted end of treatment outcome (B= 1.69, SE= .28, p<.01). RR not significant predictor in behavioural measures (p >.05). Effect size of BMI in AN subsample – d= .89.
Doyle et al. (2010)	Session 4	Dimensional -Weight gain	NA	Within-group effects	Strongest predictor of posttreatment remission was achievement of at least 2.88% weight gain by Session 4 (AUC= 0.674, p= 0.024).
Fairburn (2004)	Session 6 (Week 4)	Dimensional -Reduction of purging behaviours	NA	Between-group comparisons: treatment responders vs. non-responders	Percentage reduction in purging frequency over the first 4 weeks of treatment (r=–.38, N=201, p<0.001) significantly predicted outcome at 8-month follow-up.
Fernandez-Aranda et al. (2009)	Week 4	Dimensional -Abstinence from binging/purging	NA	Within-group effects	Presence of binging/purging at session 4 predicted poor early response (B= 1.38, p= 0.044). No predictors of abstinence at the end of treatment identified.
Grilo & Masheb (2007)	Week 4	Categorical – Reduction of binge-eating episodes by 70% or greater	42%	Between-group comparisons – rapid vs. non-rapid responders	Participants who showed rapid response were significantly more likely to achieve remission from binge eating at end of treatment vs. non-rapid responders ((χ^2=12.5, df=2, p<0.002).
Hartmann et al. (2007)	Week 4	Dimensional - Weight gain	NA	Within-group effects	Weight development between weeks 3-4 highly predictive of weight at discharge (β= .32, SE= .09, p= .001)
Hilbert et al.	Week 4	Categorical - Reduction of	73.4%	Between-group	Greater remission from binge-eating was found in rapid responders in the

(2015)		binge-eating episodes by 70% or greater	(BWL) 74.2% (CBTgsh) 65.3% (IPT)	comparisons – rapid vs. non-rapid responders	CBTgsh condition (t= 42.52, p= .01), but not in IPT (t= 2.60, p= .85) or BWL (t= 24.08, p= .14).
Hilbert et al. (2019)	Week 1 OR Week 4	Categorical – Reduction of binge eating of 10% or greater (Wk 1) OR reduction of binge eating of 70% or greater (Wk 4)	52.4% (Wk 1) 38.1% (Wk 4)	Between-group comparisons – rapid vs. non-rapid responders	Week 1 rapid responders had significantly higher rates of binge remission at EoT than non-rapid responders (χ^2(df = 1) =5.59, p = .018), but week 4 rapid responders did not (p >.05).
Kelly et al. (2014)	3 weeks	Dimensional -Reductions in EDE-Q score	NA	Within-group effects	Early Self-Compassion Change x Time significantly predicted decreases in eating disorder symptoms over the course of treatment (B=-.20, p < .01, r= .15), as did Early Shame x Time, (B=-.16, p< .01, r=.23). Larger reductions in shame/increases in self-compassion predicted larger decreases in eating disorder symptoms.
Keshen et al. (2017)	6 weeks	Dimensional -Reductions in EDE-Q score	NA	Within-group effects	Change in self-efficacy over the first six weeks of treatment inversely predicted end-of-treatment outcomes (measured by EDE-Q) (β = −0.70, t(44) = −5.77, p < .001) – i.e. early increases in self-efficacy associated with better end-of-treatment outcome.
Le Grange et al. (2008)	Session 6 (week 4)	Dimensional – reduction of binge/purge behaviours	NA	Between-group comparisons – FBT vs. IPT	Symptom reduction (measured by EDE) at session six predicted remission at posttreatment (AUC= .814, p< .001) regardless of treatment modality.
Le Grange et al. (2014)	FBT: Session 3 AFT: Session 4	Dimensional – weight gain	NA	Between-group comparisons: FBT vs. AFT	Weight gain of 2.65 kg by session 3 in FBT (AUC= .670, p= .043), and 3.20kg by session 4 in AFT (AUC= .754, p=.014) were the earliest predictors of remission at EoT. Early weight gain did not predict remission at follow-up for either treatment.
Lock et al. (2006)	Week 9	Dimensional – increases in weight	NA	Within-group effects	Change in weight at week 9 (B= .53, p= .018) significantly predicted remission at end of treatment.
MacDonald	Week 2	Categorical – four definitions	For # of	Between-group	Post-treatment (EoT) episode frequencies were significantly different

et al. (2015)	OR Week 4	used 1) One or fewer OR a 95.7% or greater reduction of binge and/or/vomit episodes in the first two weeks. 2) 3 or fewer OR a 99.7% or greater reduction of binge and/or vomit episodes in the first four weeks	episodes: 61.4% (Wk 2), 65.8% (Wk 4). For % reduction: 51.9% (Wk 2), 32.3% (Wk 4).	comparisons – groups separated based on RR definition.	between groups using all definitions, with rapid responders having lower episode frequencies than non-rapid responders. Episode frequency in the first four weeks, t(87.25)= -3.51, p= .001, d= 0.61 Episode frequency in the first two weeks, t(67.86)= -3.58, p= .001, d= 0.61 Percent reduction in the first four weeks, t(120.14)= -4.60, p < .001, d= 0.74 Percent reduction in the first two weeks, t(88.81)= -3.74, p < .001, d= 0.59 The only definition that significantly predicted longer-term remission (at 6 & 12-month follow-ups) was "3 or fewer episodes in the first four weeks".
MacDonald et al. (2017)	Session 4	Categorical – 90% or greater reduction in binge/vomit episodes from baseline	95.7% (CBT-RR) 71.4% (MI)	Between group comparisons – CBT-RR vs MI	CBT-RR group demonstrated significantly higher rate of rapid response (d= .33, p= .04). No significant difference between groups in terms of EoT outcome (t (42)= .37, p= .72, d = .11)
MacDonald & Trottier (2019)	Week 4	Dimensional – reductions in EDE score	NA	Within-group effects	Early access to emotion regulation strategies significantly predicted treatment outcome at 6-month follow up (F change(1, 47) = 10.27, p = .002, R^2 change= .16)
Marrone et al. (2009)	Session 6 (Week 4)	Dimensional – reductions in binging/purging behaviours	NA	Between-group comparisons: face-to-face vs. telemedicine CBT.	Percentage reduction in binge-eating at weeks 2,4,6 and 8 are clinically useful tools in predicting outcome at end of treatment, and at 3-month and 1-year follow-ups.
Masheb & Grilo (2007)	Week 4	Categorical – 65% or greater reduction in binge eating by session 4	54.7%	Between-group comparisons – rapid vs. non-rapid responders	Participants who showed rapid response in OBE reduction were significantly more likely to achieve remission from binge eating ($\chi^2(1)= 8.55$, $p= .003$).
Matheson et al. (2020)	By Session 10	Dimensional – reduction in binging/purging	NA	Between-group comparisons – comparing treatment	Reduction in purging at session 2 (AUC= .799, p<.001) and reduction in binge-eating at session 4 (AUC= .750, p<.01) the most significant predictors of end-of-treatment outcome regardless of treatment modality.

				modality	
Munsch et al. (2012)	Week 4	Dimensional – reduction in EDE-Q score/BMI	NA	Between-group comparisons – comparing treatment modality	Rapid response significantly predicted outcome for: EDE total score ($p<.05$), EDE eating concern ($p<0.001$), EDE shape concern, EDE weight concern & number of self-reported weekly binge-eating episodes (all $p<.01$) at six-year follow-up.
Olmsted et al. (1996)	Week 4	Categorical – three or fewer binge or vomit episodes in the first four weeks of treatment	41%	Between group comparisons: rapid vs. slow vs. partial. vs non-responders	Rapid responders had significantly reduced numbers of binge ($F(3,162)=79.23$, $p<.00001$) & vomit episodes ($F(3,162) = 101.02$, $p<.00001$) at end of treatment.
Pellizzer et al. (2019)	Session 4	Dimensional – Reductions in EDE-Q/CIA scores	NA	Within-group effects	Early change in body image flexibility significantly predicted change in global eating disorder psychopathology at EoT ($B= -.05$, $p < .001$), as did early changes in compassion ($B = -.06$, $p= .004$).
Raykos et al. (2013)	3-6 weeks	Categorical – reduction in EDE-Q global score of 1.52 or greater	34%	Between-group comparisons – rapid vs. non-rapid responders	Average time between baseline & second administration of EDE-Q was 4.6 weeks. Rapid responders required significantly fewer treatment sessions ($\chi^2= 7.54$, $p=0.007$), and had significantly lower EDE-Q global scores ($\chi^2= 16.67$, $p<0.0005$) at end of treatment. Rapid responders significantly more likely to achieve remission at EoT (χ^2 (3, N=105)= 14.20, $p=.003$, effect size=0.368).
Raykos et al. (2014)	Session 2	Dimensional – reductions in EDE-Q score.	NA	Within-group effects	Early changes in therapeutic alliance (HAQ-II) did not significantly predict EDE-Q score at end of treatment. ($\beta= -.12$, $p >.05$)
Safer & Joyce (2011)	Week 4	Categorical – 65% reduction in binge eating by session 4	41%	Between-group comparisons – rapid vs. non-rapid responders	Rapid responders significantly more likely to achieve abstinence from binge eating at end of treatment than non-responders ($\chi^2= 9.22$, $df= 1$, $p =.002$.).
Thompson-Brenner et al. (2015)	8 sessions (Week 4)	Dimensional – percentage reduction in purging by week 4	NA	Between-group comparisons – remitted vs. non-remitted	Percentage reduction in purging by session 4 significantly associated with remission at end of treatment ($t= -2.67$, $p=.011$). Sensitivity analysis showed 65% reduction to be optimal cutoff point.
Turner et al. (2015)	6 sessions	Dimensional – reduction in EDE-Q	NA	Within-group effects	Early change in dietary restraint ($t= 2.61$, $p= .011$, $\beta= .309$), eating concern ($t=2.10$, $p= .039$, $\beta= .297$) and shape concern ($t= -3.36$, $p= .001$, $\beta= -.485$) variables on the EDE-Q significantly predicted end-of treatment EDE-Q

					scores..
Turner et al. (2016)	6 sessions	Dimensional – reduction in PBQ-SF & HADS scores	NA	Within-group effects	Early changes in EDE-Q restraint predicted significant reductions across personality measures (all p<.05), and there was an overall significant effect of EDE-Q scores on depression (F (7,75)= 4.70, P < .001) and anxiety (F(7,75)= 3.33, P < .005) measures.
Vaz et al. (2014)	3 sessions	Categorical – 51% reduction in bulimic symptoms	50%	Within-group effects	Early response the only significant predictor of treatment outcome at EoT follow-up (B = -6.17, p = .004)
Wales et al. (2016)	6 weeks	Dimensional – increase in BMI	NA	Within-group effects	Meeting NICE weight guidelines within 6 weeks of starting treatment significantly predicted the likelihood of reaching a BMI of 17.5 by end of treatment (B= 2.895; p=.001).
Waller et al. (2018)	Session 4	Dimensional – Reductions in EDE-Q	NA	Within-group effects	Significant associations between early change in EDE-Q Global scores (t=2.46; p<.02) and early change in WAI-SR total scores (t=5.23; p<.001) with overall change in EDE-Q Global scores at end of treatment.
Zunker et al. (2010)	Week 1 OR Week 4	Categorical – Symptom reduction in binge-eating of 15% or greater by week 1 OR Reduction in binge-eating of 70% or greater by week 4	53.1% (Wk 1) 73.7% (Wk 4)	Between-group comparisons – rapid vs. non-rapid responders	Week 1 early responders more likely to achieve remission (AUC= .699). No significant differences between rapid/non-rapid responders at Week 4.

Meta-Analysis

Primary meta-analysis

A primary meta-analysis was conducted using *r* correlation coefficients from 26 studies (including 29 unique samples and 2,740 participants) to examine associations between early response and post-treatment outcomes. A forest plot for this meta-analysis is shown in Figure 2.

The pooled correlation coefficient was $r = 0.41$ [95% CI: 0.32-0.48], $p < .0001$, indicating a moderate but highly significant positive correlation between early response and treatment outcome. This indicates that early response is significantly correlated with better treatment outcomes.

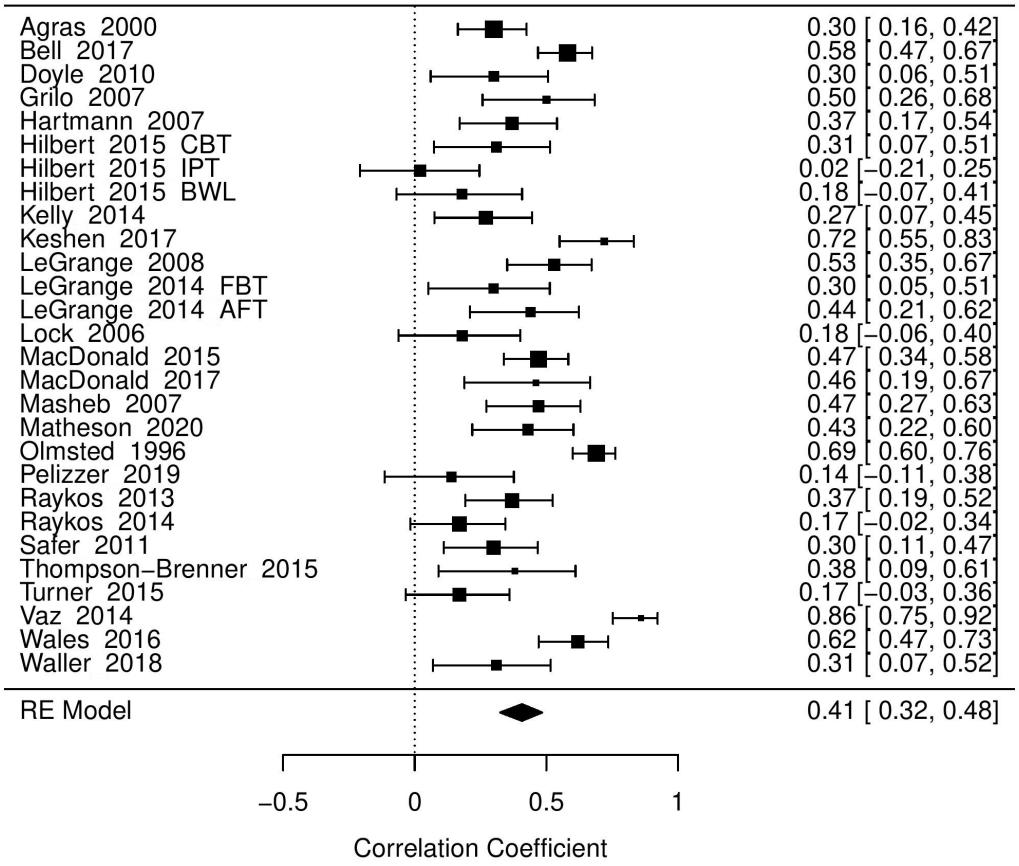

Figure 2: *Forest Plot of the Primary Meta-Analysis*

Cochrane's Q test revealed significant evidence of a large degree of heterogeneity within the sample, $Q(27) = 136.43$, $p < .0001$, $I^2 = 80.2\%$ [95% CI: 72.1%; 86.0%]. Inspection of the

funnel plots (Figure 3) showed some asymmetry of correlation coefficients, potentially indicating evidence of publication bias. However, the weight-function model likelihood ratio test did not approach statistical significance, $\chi^2(1) = .001$, p = .97, which does not confirm publication bias.

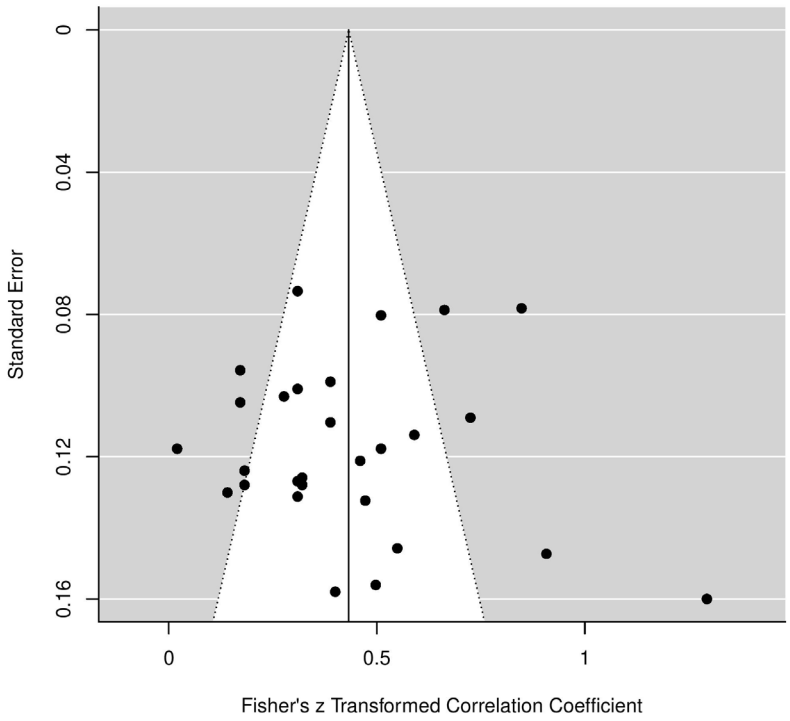

Figure 3: *Funnel Plot of the Primary Meta-Analysis*

Moderator Analyses

The pooled effect of early response was similar in RCTs and cohort studies (*r* = .34 vs. *r* = .38), and study design was not found to be a statistically significant moderator (Q(26) = 76.80, *p* = .53). Similarly, the effect of early response was not significantly stronger (Q(26) = 76.80, *p* = .17) in samples with combined treatments (psychotherapy + pharmacotherapy or dietetics) compared to purely psychological treatment (*r* = .51 vs. *r* = .36). The effect of early response was not significantly different (Q(23) = 76.80, *p* = .70) in participants with different diagnoses - bulimia nervosa (*r* = .40); anorexia nervosa (*r* = .36); and binge eating disorder (*r* = .28). Similarly, the primary treatment outcome measure was not a statistically significant moderator (Q(23) = 76.80, *p*

= .82) - BMI (*r* = .46); weight (*r* = .29); EDE-Q (*r* = .38); and EDE-I (*r* = .35). The difference in effect sizes was similar in samples using a categorical indicator of early response (*r* = .41) and those using a dimensional indicator (*r* = .33) (Q(26) = 76.80, *p* = .21). The effect of early response tended to be stronger in studies classed as at high risk of bias (*r* = .60) relative to those classed as moderate (*r* = .33) and low risk (*r* = .38), but the risk of bias classification was not a statistically significant moderator (Q(25) = 76.80, *p* = .09).

Discussion

This comprehensive review of the empirical literature in the field of eating disorders provides compelling evidence that early response to psychological treatment is significantly associated with post-treatment outcomes measured subjectively (e.g., self-reported symptoms) and objectively (e.g., body-mass index). Thirty-three papers met the criteria for inclusion, including 13 RCTs and 21 cohort studies focusing on a wide range of eating disorders. Twenty-five of those studies (with 28 treatment groups) were eligible for inclusion in a quantitative synthesis using random effects meta-analysis. The present findings converge with and extend previous findings in the field of eating disorders, providing evidence of the stability and replicability of the early response phenomenon. Such evidence, accumulated over twenty years, establishes early response as the most robust predictor of treatment outcomes in the field of eating disorders.

Summary of the evidence

The systematic review shows that the eating disorders literature has considerable divergence in the measures used and the therapies delivered (with CBT as the most commonly studied in this way). However, relatively few studies (<10%) were rated as having high risk of bias. Approximately half of patients were classified as early responders, with session 4 being the most commonly used time-point to define this. Early responders had reliably better treatment outcomes in the large majority of the studies.

It is worthy of note that the meta-analyses that have addressed this question to date (Linardon et al., 2016; Nazar et al., 2017; Vall & Wade, 2015) have used different search terms

and inclusion/exclusion criteria. As a result, they have yielded different numbers of papers for inclusion in ways that cannot be explained simply by the date of the search itself. For example, Vall and Wade (Table 2) included 12 papers that contributed to their specific meta-analysis on the impact of early change, and Linardon et al. (Table 1) included 20 such papers, though there were papers in the Linardon et al. analysis that were not included in the Vall and Wade analysis even though they would have been available. The present meta-analysis included nine papers that were published after the Linardon et al. data search, and a further six that were published prior to that date but which Linardon et al.'s inclusion criteria did not meet (though some were included in the Vall and Wade analysis). Both Linardon et al. (2016) and the present paper included more than the Nazar et al. (2017) review, due to Nazar et al. requiring a more specific indicator of outcome (diagnostic change). To summarise, the numbers of papers included in the different meta-analyses depends on both when their data searches were conducted and the specific questions being asked. However, it is important to note that the literature has progressed considerably (and at least partly as a result of) the Vall and Wade (2015) and Linardon et al. (2016) meta-analyses, with nine further eligible publications emerging since the Linardon et al. study.

It is also important to consider the assumptions made when conducting meta-analyses, to enhance comparability and replicability. Previous meta-analyses have performed separate analyses for different outcomes (e.g., Linardon et al., 2016). This approach results in meta-analyses that have relatively low statistical power due to the clustering of smaller subsets of studies, precluding the detailed subgroup analyses that we intended to perform from the outset of this project (see pre-registered intention to examine sources of heterogeneity). Pooling all or most studies together yields an overall larger sample size for meta-analysis, enabling a more robust examination of heterogeneity. One conventional option is to pool effect sizes from different measures used within each study. However, the advantages of taking a single measure with the highest effect size are that it enabled us to examine the upper-bound of the early response effect, and it enabled us to test whether this upper-bound was moderated by the specific choice of

measure (as per our pre-registered examination of heterogeneity). If one were to pool within-study effect sizes, heterogeneity in outcome measures cannot be examined in the same way, simply because one is eliminating (i.e., smoothing/averaging) this specific source of heterogeneity. This rationale was previously applied in the systematic review by Beard and Delgadillo (2019), which served as a model for the methodological choices in the present review.

The meta-analysis results indicate a moderate overall effect of early response (r = 0.41), with considerable heterogeneity. This effect is a robust one, as indicated by the fact that there were no significant moderators of the effect of early response on treatment outcomes. This overall effect is smaller than the pooled effect reported by Vall and Wade (2015) for the end of treatment (r = 0.51), though it is more similar to their pooled effect at follow-up (r = 0.35). It is more similar to the effects reported by Linardon et al. (2016) for end-of-treatment behavioural and cognitive outcomes (r = 0.397 and r = 0.288 respectively). Conversion of the Nazar et al. (2017) 'area under the curve' statistics indicates that their equivalent r-values also demonstrated similar moderate overall effect sizes ($r_{equivalent}$ = 0.21-0.46). It is possible that the lower effect sizes since the original Vall and Wade (2015) report indicates that the impact of early change is not as positive as early summaries indicated, but it is equally possible that the original effect size was a product of Vall & Wade's inclusion criteria (which did not include papers identified in the following meta-analyses). What is more consistent across the meta-analyses is the lack of evidence that moderators play a part. This meta-analysis has replicated Linardon et al.'s failure to find any such factors that limit or enhance the impact of early change on eventual treatment outcome. Regardless of the reason for any small reduction in effect size, the value of early change remains clear, making it an important clinical target, regardless of any potential factors that have been considered to date.

Comparison with the effect of early change in other disorders

These findings support the conclusion that the impact of early response to treatment is an important predictor of outcome in eating disorders (Linardon et al., 2016; Nazar et al., 2017; Vall & Wade, 2015). However, it is noteworthy that the moderate effect shown overall is less strong than

the comparable effects shown in the treatment of depression and (even more so for) anxiety (Beard & Delgadillo, 2019), where large and very large effects were shown. However, Beard and Delgadillo (2019) did not consider the impact of date of publication in their meta-analysis. Therefore, as raised above, it is possible that the impact of early change has changed over time in eating disorders alone, or it might be a more general pattern across psychological therapies for different disorders, potentially as a function of increased methodological quality. Future research on early change in different disorders and for different therapies should consider temporal stability in order to determine whether this is a specific issue for eating disorder treatment. If it is specific to eating disorders, then this might be due to improvements in the representativeness and quality of the research in that field, demonstrated by lower levels of publication bias and heterogeneity in the past five years.

Strengths and limitations of this research

This literature shows considerable variability in study design, the treatments used, the eating disorders addressed, and the measures used. As a result, the findings are characterised by a large degree of heterogeneity. The lack of clearly agreed and commonly used outcome measures in the early part of treatment and at the end of treatment is a limitation of this review. Similarly, not all of the studies accessed reported adequate data for inclusion in meta-analysis. Grey literature (e.g., posters, conference proceedings, dissertations) were excluded in order to draw conclusions from scientifically peer reviewed and therefore more rigorous and credible sources of evidence. It is not known whether accessing the grey literature would have changed the overall outcome of the review, but we did not find strong or significant evidence of publication bias in the present meta-analysis. Given that this and previous meta-analyses (Linardon et al., 2016; Vall & Wade, 2015) have identified sets of papers that do not perfectly match, we suggest that future studies should aim to use search strategies and inclusion criteria that are consistent with the existing meta-analyses, to allow fuller comparability.

The present review has several strengths, such as being pre-registered, using a range of

databases, and delineating the findings according to whether they had previously been summarised and whether they were newly reviewed. It also directly compared the outcomes of RCTs and cohort studies, allowing us to demonstrate that early treatment gains are as relevant in routine clinical practice as they are in efficacy studies, despite the likely lower levels of adherence, monitoring and close supervision in routine care.

Implications for theory, research and practice

These findings support other research in the field of therapeutic processes (e.g., Beard & Delgadillo, 2019; Linardon et al., 2016; Vall & Wade, 2015), suggesting that understanding the effectiveness of psychological therapies depends on understanding the processes that underlie early change. Despite the well-established prognostic influence of early change, the mechanisms of change that underpin early response to treatment are not well understood. Early change might be due to the effective implementation of specific change strategies (e.g., adaptive behaviour change, reappraisal), a therapeutic "remoralization" effect (as argued by Howard, Lueger, Maling, & Martinovich, 1993), or a combination thereof. More recent research in the field suggests that the early response phenomenon may - at least partly - be explained by placebo effects that are common across psychotherapeutic and wider healthcare interventions (Beard & Delgadillo, 2019).

Future research into treatment outcomes should routinely assess early outcome, using objective and subjective measures, and report on its role as a predictor of outcomes. This conclusion applies to a number of disorders, but needs to be tested in a wider range. In this review, approximately half of patients with eating disorders achieved substantial early change. That leaves the question of why the other 50% do not change early on in treatment. Further research is needed to determine whether pre-treatment patient characteristics influence early change, or whether there are clinician or service characteristics that could be addressed to enhance early response to therapy.

In clinical terms, this review and meta-analysis demonstrates that early response to treatment should be considered as a critical prognostic indicator of eating disorder treatment

outcomes, regardless of diagnosis or setting. Clinicians should be encouraged to use treatments that focus on early change (e.g., Waller, Tatham, Turner, Mountford, Bennetts, Bramwell, Dodd & Ingram, 2018; Waller, Turner, Tatham, Mountford & Wade, 2019), and to measure such symptom change around the fourth session, regardless of the planned length of treatment. Measurement of outcomes should include objective elements (e.g., bulimic behaviors; BMI), as well as more subjective aspects (e.g., EDE-Q scores). Supervision is a key element in whether clinicians focus on such early change, helping them to stay on track rather than delaying the implementation of change. However, key to promoting early change is the engagement of patients in tolerating their anxiety, particularly if they have previously had therapies that de-emphasised or explicitly avoided early change. Finally, clinicians and supervisors need to consider how to respond when patients do not show change in that early part of therapy. Not all patients with eating disorders benefit from our existing therapies, but decisions to extend therapies that are not working early on or to transfer the patient to a different therapy should be considered in light of understanding why the patient has not benefitted from the first treatment. It is known that clinician characteristics can influence whether therapy for eating disorders is extended or not (e.g., Turner, Tatham, Lant, Mountford & Waller, 2014), but patient benefit requires clinical decisions that are made on the basis of patient need rather than clinician preferences or characteristics.

Conclusion

Early symptomatic response is one of the most well-established and replicated predictors of psychological therapy outcomes, and it is the single best prognostic indicator in the specific field of eating disorders. The breadth and strength of this evidence indicates that early response should be incorporated into clinical decision-making in the treatment of eating disorders, as a way to assess progress and to guide the timely adjustment of treatment plans and duration. In particular, clinicians, supervisors and services are encouraged to focus on attaining early change, in order to attain the best possible outcome for individual patients.

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Supplementary material

A: Full search strategies used on each search engine, resulting in 415 documents.

SCOPUS

SEARCH: (TITLE-ABS-KEY (anorexia OR bulimia OR "eating disorder" OR "binge eating disorder") AND TITLE-ABS-
KEY ((early OR rapid OR sudden) W/1 (gain* OR response OR symptom* OR improvement* OR change*)) AND TITLE-ABS-
KEY (treatment OR therapy OR intervention) AND TITLE-ABS-KEY (outcome))
277 results

PSYCInfo

SEARCH:
(Anorexia OR bulimia OR “binge eating disorder” OR “eating disorder”)
AND (early OR rapid OR sudden) ADJ (gain* OR response OR symptom* OR improvement* OR change*)
AND (therap* OR treatment* OR intervention*)
AND (outcome)
54 results

PubMed

SEARCH:
(anorexia) OR bulimia OR "eating disorder" OR "binge eating disorder")
AND ((early OR rapid OR sudden) AND (gain* OR response OR symptom* OR improvement*OR change*))
AND ((psychological) AND (therap* OR treatment* OR intervention*)
AND outcome*
84 results

B. Potentially relevant studies that were identified by the search but that were excluded from the meta-analysis, with reasons for exclusion.

CITATION	*TITLE*	*DOI*	REASON(S) FOR EXCLUSION
Brockmeyer et al. (2019)	Sudden gains in Cognitive Behavioural Therapy and Focal Psychodynamic Therapy for Anorexia Nervosa: Findings from the ANTOP Study	https://doi.org/10.1159/000499118	Study fails to define early response – study focuses on sudden gains
Cartwright et al. (2017)	Sudden gains in the outpatient treatment of Anorexia Nervosa: A process-outcome study	https://doi.org/10.1002/eat.22773	Study fails to define early response – study focuses on sudden gains
Cavallini & Spangler (2013)	Sudden gains in Cognitive Behavioural Therapy for Eating Disorders	https://doi.org/10.1521/ijct.2013.6.3.292	Study fails to define early response – study focuses on sudden gains
Grilo, Masheb & Wilson (2006)	Rapid response to treatment for Binge Eating Disorder	https://doi.org/10.1037/0022-006X.74.3.602	Study includes participant groups receiving non-psychological interventions.
Grilo et al. (2015)	Predicting Meaningful Outcomes to Medication and Self-Help Treatments for Binge Eating Disorder in Primary Care: The Significance of Early Rapid Response	https://doi.org/10.1037/a0038635	Study includes participant groups receiving non-psychological interventions.
Kahn et al. (2019)	Early changes in depression predict outcomes of inpatient adolescent anorexia nervosa	https://doi.org/10.1007/s40519-019-00686-9	Some study participants fail to meet age criteria
Madden et al. (2015)	Early Weight Gain in Family-Based Treatment Predicts Greater Weight Gain and Remission at the End of Treatment and Remission at 12-Month Follow-Up in Adolescent Anorexia Nervosa	https://doi.org/10.1002/eat.22414	Primary intervention used in study is not psychotherapy based.
McFarlane, Olmsted & Trottier (2008)	Timing and Prediction of Relapse in a Transdiagnostic Eating Disorder Sample	https://doi.org/10.1002/eat.20550	Study definition of remission is based on subjective measure (adherence to a meal plan)
Schlupp, Meyer & Munsch (2005)	A Non-Randomized Direct Comparison of Cognitive-Behavioral Short and Long-Term Treatment for Binge Eating Disorder	https://doi.org/10.1159/000319538	Study uses quasi-experimental design
Swenne, Parling & Salonen Ros (2017)	Family-based intervention in adolescent restrictive eating disorders: early treatment response and low weight suppression is associated with favourable one-year outcome	https://doi.org/10.1186/s12888-017-1486-9	Some study participants fail to meet age criteria

C. Risk of bias table for observational cohort studies

First Author and Year	Issue clearly focused?	Cohort recruited acceptably?	Outcome accurately measured to minimise bias?	Confounding variables	Follow-up of subjects	Completeness of Results	Precision of Results	Believability of results	Applicability to intended population	Fit with other research	Implications of the study	Overall rating
Agras et al. (2000)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Bell et al. (2017)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Doyle et al. (2010)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Moderate risk	Moderate risk
Fairburn (2004)	Low risk	Low risk	Moderate risk	Low risk	Low risk	Moderate risk	High risk	Moderate risk	Moderate risk	Low risk	Moderate risk	High risk
Fernandez-Aranda et al. (2009)	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Hartmann et al. (2007)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Hilbert et al. (2019)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Kelly et al. (2014)	Low risk	Low risk	Low risk	Low risk	High risk	Moderate risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Keshen et	Low risk	Low risk	Low risk	Low risk	Moderate	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

al. (2017)					risk							
MacDonald et al. (2015)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
MacDonald & Trottier (2019)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Olmsted et al. (1996)	Low risk	Low risk	High risk	Moderate risk	Low risk	Low risk	High risk	Moderate risk	Low risk	Low risk	Moderate risk	High risk
Pelizzer et al. (2019)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Raykos et al. (2013)	Low risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk	Moderate risk
Raykos et al. (2014)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Turner et al. (2015)	Low risk	Low risk	Moderate risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Turner et al. (2016)	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk
Vaz et al. (2014)	Low risk	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Moderate risk	Moderate risk
Wales et al. (2016)	Low risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Low risk	Moderate risk
Waller et al. (2018)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

D. Risk of Bias table for RCTs.

FIRST AUTHOR & YEAR	Bias arising from randomisation process	Bias due to deviation from intervention	Bias due to missing outcome data	Bias due to measurement of outcome	Bias due to selective reporting of outcomes	Overall Risk of Bias
Grilo & Masheb (2007)	Low risk	Low risk	Moderate risk	Low risk	Low risk	Low risk
Hilbert et al. (2015)	Low risk	Low risk	Moderate risk	Low risk	Moderate risk	Moderate risk
Le Grange et al. (2008)	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Le Grange et al. (2014)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Lock et al. (2006)	Low risk	Low risk	Moderate risk	Low risk	Low risk	Moderate risk
MacDonald et al. (2017)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Marrone et al. (2009)	High risk	Low risk	Moderate risk	Low risk	Moderate risk	High risk
Masheb & Grilo (2007)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Matheson et al. (2020)	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Moderate risk
Munsch et al. (2012)	Low risk	Low risk	Moderate risk	Low risk	Low risk	Moderate risk
Safer & Joyce (2011)	Moderate risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk
Thompson-Brenner et al. (2015)	Low risk	Low risk	Moderate risk	Moderate risk	Low risk	Moderate risk
Zunker et al. (2010)	Low risk	Moderate risk	Low risk	Low risk	Moderate risk	Moderate risk