## REVIEW

## EATING DISORDERS WILEY

## Residual eating disorder symptoms and clinical features in remitted and recovered eating disorder patients: A systematic review with meta-analysis

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### Abstract

**Objective:** In psychiatry, the presence of residual symptoms after treatment is linked to the definitions of remission and recovery. To identify the presence of residual eating disorder (ED) symptoms and associated non-ED clinical features in remitted and recovered EDs, the current systematic review with meta-analysis was performed.

**Method:** A systematic review was conducted on residual ED symptoms and non-ED clinical features including comorbid psychopathology, neurophysiological functioning, cognitive functioning, and quality of life in ED patients considered remitted or recovered. To examine residual ED symptoms, meta-analyses were performed while considering age, study quality, remission, and recovery criteria strictness as moderators. Sensitivity, publication bias, and heterogeneity analyses were also conducted.

**Results:** The 64 studies selected for the systematic review underscored the presence of residual ED symptoms in anorexia nervosa (AN) and bulimia nervosa (BN), and impairments and deficits in the additional features examined. From the 64 studies, 31 were selected regarding residual ED symptoms in AN for meta-analysis. Large effect sizes indicated that remitted/recovered AN patients reported significantly lower body mass index (Hedges' g = -0.62[-0.77, -0.46]) and significantly greater symptomatology in terms of ED examination-questionnaire (Hedges'g = 0.86 [0.48,1.23]) and ED inventory (Hedges' g = 0.94[0.64,1.24]) than healthy controls, independently of remission and recovery criteria strictness, age, and study quality.

**Discussion:** The presence of residual ED symptoms in AN is quantitatively supported, whereas the presence of residual ED symptoms in BN should be further investigated. Data on binge-eating disorder are missing. Future research should use consistent, multicomponent, and standardized comparable indicators of recovery.

### Resumen

**Objetivo:** En psiquiatría, la presencia de síntomas residuales después de tratamiento está ligado a las definiciones de remisión y recuperación. Para identificar la presencia de síntomas residuales del trastorno de la conducta alimentaria (TCA) y características clínicas no de TCA asociadas en pacientes remitidos y recuperados de TCAs, se realizó la presente revisión sistemática con meta-análisis.

**Método:** Se realizó una revisión sistemática en síntomas residuales de TCA y en características clínicas no de TCA incluyendo psicopatología comórbida, funcionamiento neurofisiológico, funcionamiento cognitivo, y calidad de vida en pacientes con TCA considerados remitidos o recuperados. Para examinar los síntomas residuales de TCA se realizaron meta-análisis considerando edad, calidad del estudio, criterios de remisión y recuperación estrictos como moderadores. También se realizaron análisis de sensibilidad, sesgo de publicación y heterogenicidad.

Resultados: Los 64 estudios seleccionados para la revisión sistemática destacaron la presencia de síntomas residuales de TCA en anorexia nervosa (AN) y bulimia nervosa (BN), y alteraciones y déficits en las características adicionales examinadas. De los 64 estudios, 31 fueron seleccionados para meta-análisis por los síntomas residuales de TCA en AN. Las medidas de efecto mayor indicaron que los pacientes remitidos/ recuperados de AN reportaron índices de masa corporal significativamente menores (Hedges' g = -0.62[-0.77,-0.46]) y significativamente mayor sintomatología en términos del Cuestionario de Evaluación de TCA (Eating Disorder Examination-Questionnaire) (Hedges' g = 0.86 19 [0.48,1.23]) y el Inventario de TCA (Eating Disorder Inventory) (Hedges' g= 0.94[0.64,1.24]) que los controles sanos, independientemente de lo estricto de los criterios de remisión y recuperación, edad y calidad del estudio. Discusión: La presencia de síntomas residuales de TCA en AN es apoyada cuantitativamente, mientras que la presencia de síntomas residuales de TCA en BN necesita ser investigada a mayor profundidad. Los datos en trastorno de atracones están ausentes. Las investigaciones futuras deberían utilizar indicadores de recuperación consistentes, de múltiples componentes y estandarizados.

#### KEYWORDS

assessment, eating disorders, recovery, remission, residual symptoms, staging

### 1 | INTRODUCTION

Historically, in psychiatry, the medical model has been the theoretical framework of reference to conceptualize mental illness (Mountain & Shah, 2008) as well as to define recovery states (Andresen, Oades, & Caputi, 2011). The medical model implies that an underlying pathology explains and causes signs and observable symptoms, which are the manifestation of the disorder, but not the illness itself. In such conventional approaches, remission refers to the absence of signs and symptoms, but the underlying pathology may remain. When the underlying pathology is absent, recovery has been achieved with a return to premorbid functioning (Roberts & Wolfson, 2004).

Eating disorders (EDs) are associated with serious consequences for health, relationships, and global functioning. Such disorders are characterized by a complicated course of illness. Although there is support for favorable outcomes for most patients with EDs, both threshold and subthreshold forms may persist for more than a decade after diagnosis (Fichter, Quadflieg, Crosby, & Koch, 2017; Keel & Brown, 2010; Keel, Mitchell, Miller, Davis, & Crow, 1999). Remission rates are inconsistent ranging from 3% to 96%. The consensus is that these variations are due to discordant definitions of remission and recovery (Ackard, Richter, Egan, & Cronemeyer, 2014), mostly conceptualized within the medical model.

A recent review (Bardone-Cone, Hunt, & Watson, 2018) analyzing contemporary formulations of both ED recovery and remission underscores that such terms are used interchangeably and how both are primarily based on the absence of ED diagnosis or eating-related behaviors, that is, the observable signs and symptoms (Bardone-Cone et al., 2010; Khalsa, Portnoff, McCurdy-McKinnon, & Feusner, 2017; de Vos et al., 2017). Recovery criteria may vary in minimum body mass index [BMI] required, type of ED behaviors which must be absent, and duration of recovery. At times, the definition of recovery goes beyond the medical model, by including psychological components of ED symptoms measured mainly with the eating disorders examination (EDE) and EDEquestionnaire (EDE-Q; Bardone-Cone et al., 2010, 2018; Kordy et al., 2002). Remission from EDs, which also has been found to vary in definitions and to be inconsistently applied across studies (Ackard, Richter, Egan, & Cronemeyer, 2014), appears to not differ greatly from recovery criteria (Bardone-Cone et al., 2018). As in recovery, at times, it includes a psychological component in terms of ED symptom improvements in a standardized measure. However, remission studies frequently do not clearly state the required duration (Bardone-Cone et al., 2018).

Comprehensive and strict definitions of remission and recovery which include physical, behavioral, and psychological criteria have been reviewed (Ackard, Richter, Egan, & Cronemeyer, 2014), with the recommendation to use Bardone-Cone et al.'s (2010) criteria. More recently, further recommendations suggest including improvements in quality of life and psychological well-being within the psychological criteria, taking into account the subjective experience of recovery from the patients' perspective (Ackard, Richter, Egan, Engel, & Cronemeyer, 2014; De Vos et al., 2017) also proposed by recovery models (Andresen et al., 2011; Mountain & Shah, 2008; Roberts & Wolfson, 2004). Despite the current efforts in finding a consensus on strict ED remission and recovery criteria, the use of the conventional medical model which, in defining remission as the absence of signs and symptoms still allows the underlying pathology to be present, may be controversial (Cosci & Fava, 2013; Fava, 1996). Data suggest that the presence of residual symptoms, defined as the perseverance of symptoms and signs despite meeting remission or recovery criteria, are frequent after completion of drug or psychotherapeutic treatment in various psychiatric illnesses such as schizophrenia, unipolar depression, bipolar, panic, substance use, and EDs (Cosci & Fava, 2013; Fava, 1996). Indeed, partial remission is the most common ED outcome after treatment, whereas full remission or recovery is quite rare (Bardone-Cone et al., 2018; Kordy et al., 2002).

The assessment of residual symptoms may be particularly important in EDs, as such symptoms are associated with a high risk of relapse (Kordy et al., 2002; Vall & Wade, 2015). Symptom persistence after treatment is predictive of relapse in both anorexia nervosa (AN) and bulimia nervosa (BN; Richard, Bauer, Kordy, & COST, 2005). Relapse rates of AN range from 9% to 52% following treatment (Khalsa et al., 2017), whereas 50% of BN patients relapse by followup (Yu, Agras, & Bryson, 2013). Moreover, the highest risk of relapse falls within the first 6 or 7 months after achieving partial remission for both AN and BN patients (Richard et al., 2005). However, such residual symptoms are not considered in traditional psychiatric diagnostic frameworks as threshold manifestations and therefore are not deemed clinically significant (Cosci & Fava, 2013; McGorry, Hickie, Yung, Pantelis, & Jackson, 2006). Although the National Institute for Health and Care Excellence (National Health Service, 2017) and the American Psychiatric Association (APA, 2010) guidelines provide indications on ED assessment, identifying ED symptoms and behaviors, psychiatric status, and recommending monitoring of medical status, such guidelines do not offer recommendations for monitoring residual ED symptoms and other clinical aspects in EDs.

Considering both the importance of residual ED symptoms and how such symptoms might be inextricably linked to the definitions of ED remission and recovery, the first aim of the current work is to provide a meta-analysis to examine residual ED symptoms in ED patients while taking into account the strictness of the remission or recovery criteria applied by study authors. The second aim is to systematically review the literature on other non-ED but related symptoms and clinical features in remitted or recovered EDs. A more comprehensive farreaching overview of the clinical characterization of remitted or recovered ED patients will help to better describe the course of illness and inform clinicians on assessment strategies.

### 2 | METHOD

#### 2.1 | Information sources and searches

Pubmed and PsycINFO were systematically searched for original empirical articles utilizing the keywords *residual* OR *relapse* OR *remiss\** OR *remit\** OR *recover\** OR *subclinical* OR *subthreshold* OR *sub-syndromal*, combined through the Boolean operator AND with Anorexia nervosa, Bulimia nervosa, Binge-eating disorder. Studies were published between January 2005 and December 2018 in peerreviewed journals. Titles and abstracts were screened by one author (F.S.). Articles that appeared potentially relevant were retrieved and reviewed by two authors (E.T. and L.T.) who independently assessed each of the full reports, arriving at a consensus regarding eligibility. The methodology applied followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009).

### 2.2 | Eligibility criteria and data extraction

Inclusion and exclusion criteria and data extraction were based on patient. intervention, comparison, outcome, and study design criteria (Centre for Reviews and Dissemination, 2006). Eligible articles were in the English language and were selected for inclusion if the sample was composed of ED patients evaluated with DSM III-R, DSM-IV, DSM IV-TR, or DSM 5 (APA, 1987, 1994, 2000, 2013) in any study design and setting. During the electronic search, studies were excluded for the following reasons: the sample was composed of medically ill patients with pathologies not related to EDs; authors did not provide remission or recovery criteria; the article was a review, a case study, opinion statement, letter to the editor, a book, a dissertation, meta-analysis, or progress report. Remaining studies received full-text review to determine a final selection. For additional inclusion and exclusion criteria, see Table 1. Data were extracted on ED patients considered in partial or full remission or recovered by authors and for which remission or recovery criteria were provided, and for outcomes, referred to modifications over time or differences compared to healthy controls in five main ED outcome areas of clinical interest as underscored by the ED literature: (a) residual ED symptomatology (Vall & Wade, 2015); (b) comorbid psychiatric symptoms and psychopathology (Godart et al., 2007; Wonderlich & Mitchell, 2001); (c) neurophysiological functioning (Kaye, 2008); (d) cognitive functioning (Kanakam & Treasure, 2013; Seitz, Konrad, & Herpertz-Dahlmann, 2018); and (e) quality of life and positive mental health (de Vos et al., 2017). A table for studies reporting residual ED symptoms and other non-ED outcome areas of clinical interest in remitted/recovered ED patients includes the following: author, cases (n), percentage females, diagnostic group and diagnostic instrument, mean age in years, study design, intervention, outcomes and relevant findings, remission, or recovery criteria (see Table S1).

PICOS	Inclusion criteria	Exclusion criteria	Data extraction	<b>TABLE 1</b> Inclusion and exclusion criteria and data extraction on the			
Patient	<ul> <li>All ages</li> <li>Female, male, or mixed gender studies</li> <li>Diagnosis of AN (restrictive or binge/purge subtypes), BN, or BED</li> <li>Considered by the authors partially or full remitted or recovered from an ED</li> <li>Remission or recovery criteria provided</li> </ul>	<ul> <li>Sample composed of medically ill patients with pathologies not related to EDs</li> </ul>	<ul> <li>Study population:</li> <li>Number of participants</li> <li>Sex</li> <li>Mean age</li> <li>Diagnosis of AN, BN, or BED when reported</li> <li>Remission criteria</li> </ul>	identification of residual ED symptom: and related non-ED symptoms in EDs			
Intervention			Treatment     information when     available				
Comparison group	• Studies with or without a comparison group		Allocate into groups     where applicable				
Outcome	<ul> <li>Disorder-related ED symptomatology</li> <li>Comorbid psychiatric symptoms and psychopathology</li> <li>Neurophysiological functioning</li> <li>Cognitive functioning</li> <li>Quality of life and positive mental health</li> </ul>		<ul> <li>Modifications over time or differences compared to healthy controls in the five inclusion criteria outcome areas</li> </ul>				
Study design	<ul> <li>Prospective or Retrospective cohort, cross-sectional, case– control, or RCT</li> <li>Any length of follow-up</li> <li>Studies conducted in any setting</li> <li>English language</li> </ul>	<ul> <li>Review</li> <li>Case studies</li> <li>Opinion statements</li> <li>Letter to the editor</li> <li>Book</li> <li>Dissertation</li> <li>Meta-analysis</li> <li>Progress report</li> </ul>	<ul><li>Study design</li><li>Study setting</li></ul>				

Abbreviations: AN, anorexia nervosa; BED, binge-eating disorder; BN, bulimia nervosa; ED, eating disorder; PICOS, patient, intervention, outcomes, study design; RCT, randomized control trials.

#### 2.3 | Quality assessment and risk of bias

A customized checklist (Table S2) adapted from the National Institutes of Health, "quality assessment tool for observational cohort and controlled intervention studies" was applied (National Institutes of Health, 2014). Studies were rated as strong, moderate, or weak based on 13 criteria. The sum of ratings was used to calculate total points and assign an overall score of strong, moderate, or weak quality studies (Table S3).

### 2.4 | Methods of meta-analysis

Studies that report data on comparable outcomes regarding residual ED symptomatology were identified. Thus, the systematic review was integrated with a quantitative synthesis, by applying meta-analytic procedures (Cooper, 2010; Cooper, Hedges, & Valentine, 2009; Lipsey & Wilson, 2001). Data on other non-ED outcome areas of clinical interest, that is, comorbidity, neurophysiological and cognitive functioning, quality of life, and positive mental health, were excluded from the meta-analysis as they may be risk or vulnerability factors or may emerge as consequences of EDs and may not be understood as residual ED symptoms per se.

Statistical analyses were conducted with the meta-analytic software ProMeta 3.0. First, an effect size was computed for each study. Hedges' g (standardized mean difference) effect sizes were computed for each outcome. The Hedges' g effect size was chosen as a conservative estimate to correct for the fact that some studies may have small sample sizes (Borenstein, Hedges, Higgins, & Rothstein, 2009). Hedges' g values of |0.20|, |0.50|, and |0.80| can be interpreted as small, medium, and large effects, respectively (Cohen, 1988; Ellis, 2010). For each effect size, its 95% confidence interval, variance, SE, and statistical significance were computed. Second, effect sizes were pooled across studies for obtaining an overall effect size for each outcome with the inverse-variance method. The random-effects model was used as a conservative approach to account for different sources of variation among studies (i.e., within-study and between-studies variance) and to allow generalization of the meta-analytic findings beyond the studies included in the current synthesis (Hedges & Vevea, 1998). Third, sensitivity analyses and publication bias analyses were conducted to examine the robustness of the meta-analytic results through multiple methods (Rothstein, Sutton, & Borenstein, 2005): Fail safe N (Rosenthal, 1979); trim and fill method (Duval, 2005; Duval & Tweedie, 2000); and Egger's test (Egger, Davey Smith, Schneider, & Minder, 1997). Fourth, heterogeneity analyses were conducted using both Q and  $l^2$  statistics (Huedo-Medina, Sánchez-Meca, Marin-Martinez, & Botella, 2006). A significant Q value indicates the lack of homogeneity of results among studies.  $l^2$ estimates the proportion of observed variance that reflects real differences in effect sizes, with values of 25%, 50%, and 75% that might be considered as low, moderate, and high, respectively (Higgins, Thompson, Deeks, & Altman, 2003). Finally, moderator analyses were performed to test which factors could explain variations of results across studies (Crocetti, 2016). Meta-regressions and subgroup analyses were performed to test numerical (i.e., patients' mean age and study quality) and categorical (i.e., remission criteria strictness) moderators, respectively.

### 3 | RESULTS

### 3.1 | Selection of articles and study characteristics

Combining Anorexia nervosa with the other keywords across the two databases yielded: 847 in Pubmed 645 in PsycINFO. Combining

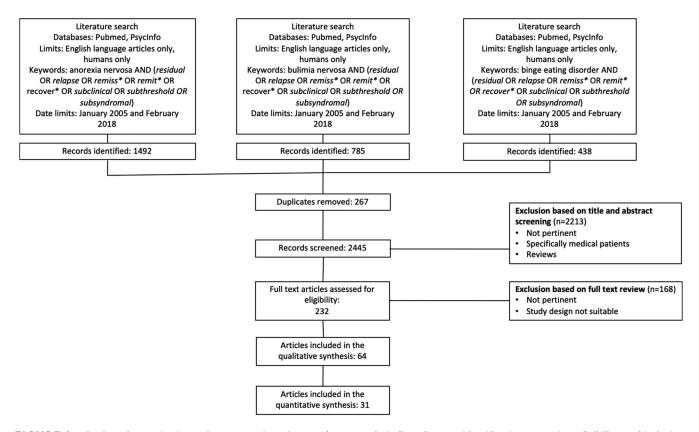
*Bulimia nervosa* with the other keywords across the two databases yielded: 422 results in Pubmed and 363 in PsycINFO. Combining *Binge-eating disorder* with the other keywords across the two databases yielded: 229 results in Pubmed and 209 in PsycINFO.

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After eliminating duplicates (n = 267), the initial screening of titles and abstracts of 2,445 references was done and it led to the exclusion of 2,213 articles. Full-text review of the resulting 232 articles led to the exclusion of 168 articles. A total of 64 studies were identified for inclusion in the review (See flow chart in Figure 1), and 31 of them were included in the meta-analytic review (information on selected studies are presented in Table S1).

With regard to study characteristics, a few results are worthy of note. Most participants of the studies were females with the exception of three, which included a small percentage of males (2.4–3.6%) (Byrne, Fursland, Allen, & Watson, 2011; Lo Sauro, Castellini, Lelli, Faravelli, & Ricca, 2013; Talbot, Hay, Buckett, & Touyz, 2015). Diagnostic information was available in most studies, with AN and BN as the most prevalent diagnosis. Only one study (Tomba, Tecuta, Schumann, & Ballardini, 2017) included binge-eating disorder (BED) in the ED sample. The majority of the selected studies were crosssectional and focused on comparing ED patients in partial or full remission or recovery with healthy controls and/or acutely ill counterparts after inpatient treatment. Half of the studies did not report specific modalities and setting of treatment.

Both "remission" and "recovery" were defined in varying ways, from weight restoration to full recovery. Several studies utilized specific



**FIGURE 1** Preferred reporting items for systematic reviews and meta-analysis flow diagram: Identification, screening, eligibility, and inclusion of data sources for the study

remission criteria considered minimal, moderate, or strict (Ackard, Richter, Egan, & Cronemeyer, 2014). Thirteen studies were found to apply strict criteria, eight of which utilized Bardone-Cone et al.'s (2010) strict criteria for ED recovery, a comprehensive definition which includes diagnostic (no current ED according to DSM), physical BMI  $\leq$  18.5 kg/m<sup>2</sup>), behavioral (full absence of binging, purging, and fasting behavior), and psychological (within 1 SD of norms on a well-established measure focused on ED cognitions) components of recovery. Twenty-three used moderate criteria among which Kordy et al.'s (2002), Morgan and Hayward's (1988), or Pike's (1998) definitions. About 40% (28 studies) used minimally strict remission criteria as defined by Ackard, Richter, Egan, and Cronemeyer (2014). Remission and recovery criteria used in the selected studies are provided in Table S1 in order of increasing strictness. In terms of risk of bias and quality assessment of selected studies, four studies were found to be of stronger quality, 26 moderate quality, and 34 of weaker quality (Table S3).

## 3.2 | Results of meta-analysis on residual ED symptoms

From the 64 selected studies for the systematic review, 31 were synthesized also quantitatively by means of meta-analytic methods. The selected studies were comparable in terms of patient diagnosis, all of which included remitted/recovered AN patients. Studies presented comparisons to control groups in BMI and ED symptomatology measured through standardized quantitative measures (EDE-Q and eating disorder inventory [EDI] total scores) and were cross-sectional in design. In terms of remission and recovery criteria, 5 studies used minimally strict criteria, 20 moderately strict, and 6 strict criteria. In terms of study quality, 14 were of weak quality, 16 were of moderate quality, whereas 1 was of strong quality (Table 2). A few studies reported on ED symptomatology in remitted/ recovered BN, measured with different instruments (EAT-26, EDI-2, and EDE-Q subscales). Only one study included BED patients. Thus, a meta-analysis procedure was not attempted for BN and BED diagnostic groups, because running analyses with less than five studies for each outcome would yield less precise estimates of the variance between studies (Borenstein et al., 2009; Cooper, 2010; Cooper et al., 2009; Lipsey & Wilson,

2001). Although 12 reported BMI in remitted or recovered BN, this datum was not included in the meta-analysis on residual ED symptoms, as it is not considered a criterion for BN (APA, 2013).

An effect size was computed for each study, to quantify the magnitude of the difference between remitted/recovered AN patients and control comparisons on BMI, ED severity, and symptomatology (EDE-Q and EDI). From the data extracted from the articles (i.e., means, SDs, and sample size of each group or p values from t tests when other data were not available), Hedges' g effect estimates for each study were computed. These results are displayed in three forest plots, one for each outcome (Figures 2-4).

Effect sizes were pooled across studies and indicated that remitted/recovered AN patients reported levels of BMI significantly lower than those of healthy controls (see Table 2). This overall effect, obtained from 31 studies involving a total of 2,167 participants, was moderateto-large. In addition, remitted/recovered AN patients reported significantly higher ED severity and symptomatology, measured with the EDE-Q and EDI, than healthy controls. Both effects (obtained from seven and five studies, respectively; Table 2) were large.

Sensitivity analyses and publication bias analyses pointed to the robustness of these meta-analytic results. In fact, results discussed above did not change substantially when removing any study from the analyses and they were not affected by publication bias (see Table 2), as indicated by the convergent results of multiple methods (Fail safe N, trim and fill method, and Egger's test).

The heterogeneity analyses conducted using both Q and  $I^2$  statistics indicated that the overall results obtained for BMI and EDE-Q measured symptomatology were characterized by significant heterogeneity, which was moderate-to-large and large, respectively (see Table 2), whereas the results regarding EDI measured symptomatology were homogeneous across studies.

Moderator analyses and meta-regressions highlighted that the patients' age did not affect significantly the results obtained for BMI (B = -0.00, p = .960), EDE-Q symptomatology (B = 0.06, p = .366), and EDI symptomatology (B = 0.01, p = .946). Similarly, the study quality did not moderate results obtained for BMI (B = -0.03, p = .257), EDE-Q symptomatology (B = -0.04, p = .366), and EDI symptomatology (B = -0.13, p = .211). In addition, a subgroup analysis

	Summary statistics					Heterogeneity		Assessment of publication bias			
Outcomes		N <sub>tot</sub>	N <sub>patients</sub>	N <sub>controls</sub>	Hedges' g	[95% CI]	Q	1 <sup>2</sup>	Fail safe n	Trim and fill (n of trimmed studies; estimated g, 95% Cl)	Egger's test
BMI	31	2,167	843	1,324	-0.62***	[-0.77, -0.46]	80.76***	62.85	1,301	0	0.39
Eating symptomatology (EDE-Q)	7	567	208	359	0.86***	[0.48, 1.23]	22.86***	73.75	125	2 (0.64*** [0.26, 1.03])	2.01
Eating symptomatology (EDI)	5	280	125	155	0.94***	[0.64, 1.24]	5.64	29.11	68	1 (0.83**** [0.48, 1.19])	2.59

Abbreviations: BMI, body mass index; CI, confidence interval; EDE-Q, eating disorders examination-questionnaire; EDI, eating disorders inventory; k, number of studies; N, total number of participants.

p < .05; p < .01; p < .01; resp < .001.

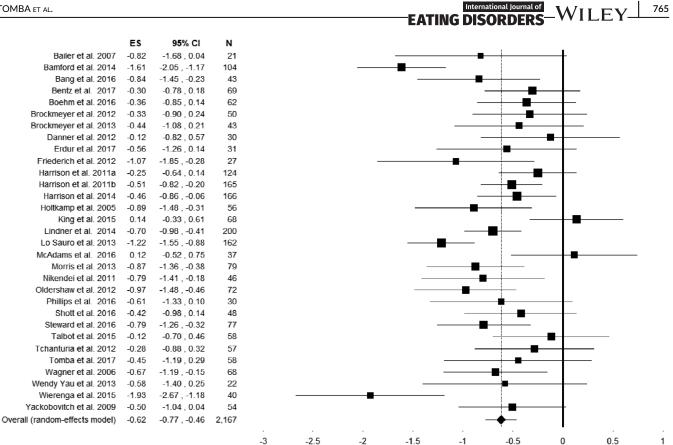


FIGURE 2 Forest plot of ESs for BMI. BMI, body mass index; CI, confidence interval; ES, effect size

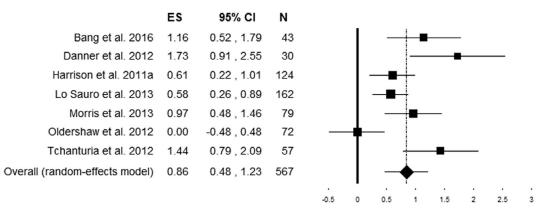
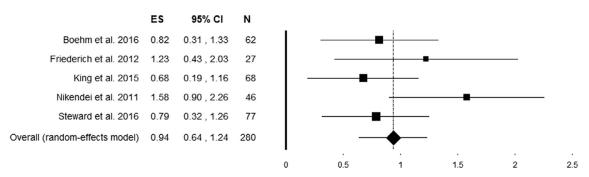
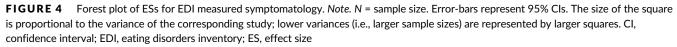


FIGURE 3 Forest plot of ESs for EDE-Q measured symptomatology. CI, confidence interval; EDE-Q, eating disorders examinationquestionnaire; ES, effect size





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was conducted on BMI to test for the effect of the categorical moderator related to remission criteria strictness. This analysis was conducted for BMI (not eating severity and symptomatology) because a good practice is to have at least three studies for each level of the moderator (Crocetti, 2016), a requirement that was respected only for BMI. Although this analysis did not yield an overall significant result, Q(2) = 0.18, p = .916, the findings for each level of the moderator, in terms of size of each effect and its precision, are worthy of attention (Cumming, 2012, 2014; Kline, 2013). Indeed, they indicate that the difference between remitted/recovered AN patients and healthy controls in BMI was larger and with higher variance (as indicated by a larger confidence interval) in studies that used minimal remission criteria (k = 5, Hedges' g = -0.73 [-1.39, -0.07], p = .029) compared to studies that adopted moderate (k = 20, Hedges' g = -0.59 [-0.76, -0.42], p = .000) or strict (k = 6, Hedges' g = -0.58 [-0.91, -0.25], p = .001) remission criteria.

## 4 | RESULTS OF THE SYSTEMATIC REVIEW **ON RESIDUAL ED SYMPTOMS AND NON-ED CLINICAL FEATURES**

#### 4.1 | Residual ED symptoms

In the reviewed studies, eating disordered behaviors in both remitted or recovered AN and BN were found. The majority of remitted and recovered AN and BN patients exhibited an improved BMI, which however was significantly lower compared to that of healthy controls (see also Table 2, meta-analytic results). In recovered AN and BN patients, core ED symptoms such as drive for thinness, obsessive-compulsive eatingrelated symptoms, oral control, restraint, caloric food restriction, food preoccupations, worsening of orthorexia nervosa symptoms, and excessive exercise were greater compared to healthy controls (Bailer et al., 2007; Bardone-Cone, Higgins, et al., 2016; Ruiz-Prieto, Bolaños-Ríos, & Jáuregui-Lobera, 2013). However, fully recovered ED patients did not differ significantly from healthy controls in exercise-related thought patterns (Bardone-Cone, Higgins et al., 2016). Indeed, in one study, binge-eating and compensatory behaviors such as self-induced vomiting, laxative use, and driven exercise ceased only in 45.7% of the total sample, which included both treatment completers and remitted patients (both AN and BN) by the end of treatment (Byrne et al., 2011).

Concerning AN, when AN patients were classified as weightrestored, eating-related psychopathology was worse compared to both healthy controls and fully recovered patients (Talbot et al., 2015). Moreover, such patients exhibited greater body checking and avoidance behaviors, as well as greater body anxiety, not differing significantly from low-weight AN patients (Bamford, Attoe, Mountford, Morgan, & Sly, 2014). Similarly, remitted and recovered AN participants scored higher than healthy controls on all eating-related symptoms such as body dissatisfaction, drive for thinness, dieting, lower caloric and fat intake, bulimia, and oral control (Bang, Rø, & Endestad, 2016; Bernardoni et al., 2016; Boehm et al., 2016; Frank, Shott, Hagman, & Mittal, 2013; Friederich et al., 2012; Harrison, Tchanturia, & Treasure, 2011; King et al., 2015; Lo Sauro et al., 2013; McAdams et al., 2016; McAdams &

Krawczyk, 2011; Nikendei et al., 2011; Phillips, Jimerson, Pillai, & Wolfe, 2016; Schebendach et al., 2011; Shott, Pryor, Yang, & Frank, 2016; Steward et al., 2016; Tchanturia et al., 2012) or were found to not improve in ED symptoms (Haynos, Roberto, Martinez, Attia, & Fruzzetti, 2014). Sustained weight-restored AN patients did not differ significantly from acutely ill AN patients in body shape dissatisfaction (Harper, Brodrick, Van Enkevort, & McAdams, 2017). In one study, recovered AN patients were found to not differ significantly in ED symptoms compared to healthy controls (Bentz et al., 2017).

Regarding BN, remitted BN patients demonstrated significant reductions in self-reported symptoms of bulimia (Steiger et al., 2005), binge-eating and vomiting episodes, external eating, laxative use, as well as reduced body dissatisfaction, interoceptive awareness, compulsivity, and drive for thinness (Meule, von Rezori, & Blechert, 2014; Steiger et al., 2005), but such symptoms were greater when compared to controls (Steiger et al., 2005). However, in one study, recovered BN patients were found to not differ significantly from controls in ED symptoms in general (Pichika et al., 2012). Moreover, remitted BN patients showed reduced food addiction behaviors according to the Yale food addiction scale, which measures addiction behaviors toward food using DSM 5 diagnostic criteria for substance use disorders, which however, along with emotional eating, was significantly more severe or more frequent compared to healthy controls (Meule et al., 2014). Remitted BN patients showed reduced dietary restraint and eating pathology compared instead to actively ill BN patients in one study (Daley, Jimerson, Heatherton, Metzger, & Wolfe, 2008) but significantly more eating concerns and body image concerns compared to never-ill women or healthy controls in other studies (Morgan, Wolfe, Metzger, & Jimerson, 2007). Moreover, a third of remitted BN patients were found to fulfill criteria for a food addiction (Meule et al., 2014).

## 4.2 | Comorbid psychiatric symptoms and psychopathology

EDs symptoms related to psychiatric comorbidity and psychopathology that may endure or emerge after treatment were: negative affect, primarily depression and anxiety, body anxiety, and obsessivecompulsive symptoms, all of which were reduced, suggesting an improvement, but did not return to normative healthy levels (Byrne et al., 2011; Wagner et al., 2006). However, such patients may have lower psychopathology to begin with. Personality traits such as higher trait anxiety, perfectionism and harm avoidance, social emotional difficulties, sensitivity to punishment, and lower reward reactivity (Bailer et al., 2007; Harrison, Treasure, & Smillie, 2011; Tarrega et al., 2014) were found in remitted ED patients. Moreover, in an additional study, treated and remitted ED patients showed no overall improvements on measures of perfectionism or mood intolerance at the end of treatment (Byrne et al., 2011).

In AN, weight-restored or recovered AN patients showed higher depression, anxiety, body image anxiety, and obsessive-compulsive symptomatology compared to healthy controls or were found to not differ significantly from acutely ill AN patients is numerous studies (Bamford et al., 2014; Bang et al., 2016; Brockmeyer et al., 2012; Buehren et al., 2011; Danner et al., 2012; Frank et al., 2013; Friederich et al., 2012; Harper et al., 2017; Harrison, Tchanturia, & Treasure, 2011; Haynos et al., 2014; Holtkamp, Müller, Heussen, Remschmidt, & Herpertz-Dahlmann, 2005; King et al., 2015; Lindner, Fichter, & Quadflieg, 2014; Lo Sauro et al., 2013; McAdams et al., 2016; McAdams & Krawczyk, 2011; Morris, Bramham, Smith, & Tchanturia, 2013; Shott et al., 2016; Tchanturia et al., 2012; Wagner et al., 2006; Yackobovitch-Gavan et al., 2009). However, in contrast, in a few studies, patients improved in psychological distress, depression, and anxiety, not differing significantly from healthy controls (Oldershaw et al., 2012; Harney, Fitzsimmons-Craft, Maldonado, & Bardone-Cone, 2014; Bernardoni et al., 2016; Bentz et al., 2017; Erdur, Weber, Zimmermann-Viehoff, Rose, & Deter, 2017) specifically when considered fully recovered (Harney et al., 2014).

Remitted AN patients compared to healthy controls exhibited dysfunctional personality traits such as greater perfectionism, compulsivity, a tendency toward inhibition (restricted expression and intimacy problems), trait anxiousness, and affective liability, punishment sensitivity, and harm avoidance (Danner et al., 2012; Friederich et al., 2012; Lindner et al., 2014; Shott et al., 2016; Yau et al., 2013). However, in one study, obsessive-compulsive traits and impulsiveness in fully recovered AN did not differ significantly from healthy controls (Lindner et al., 2014). Alexithymia was found to be greater in recovered AN compared to controls in one study (Tchanturia et al., 2012) and not differ significantly between sustained weight-restored AN and acutely ill AN patients in another (Harper et al., 2017). Schizotypal features such as suspiciousness, intimacy and identity issues, interpersonal inhibition, and social avoidance (Holliday, Uher, Landau, Collier, & Treasure, 2006; McAdams & Krawczyk, 2011) were found to improve in AN but were elevated compared to controls and not differ significantly from acutely ill patients. Concurrently, AN patients achieving weight recovery reported significantly more interpersonal difficulties than fully recovered patients and healthy controls (Talbot et al., 2015). Social anhedonia and difficulties in work and social life improved in recovered AN patients, but such changes did not reach normative levels (Harrison, Mountford, & Tchanturia, 2014; Tchanturia et al., 2012).

In recovered and remitted BN patients, negative affect such as depression, state anxiety, as well as compulsivity (Bailer et al., 2011; Daley et al., 2008; Meule et al., 2014; Morgan et al., 2007; Steiger et al., 2005; Wagner et al., 2006), obsessive-compulsive symptoms (Bailer et al., 2007; Morgan et al., 2007; Wagner et al., 2006) persisted or emerged. In a few studies, levels of anxiety, depression, and obsessions were instead not significantly different compared to healthy controls (Pichika et al., 2012). Harm avoidance and impulsivity was also found to be greater in remitted BN than in healthy controls in one study (Bailer et al., 2011) but not in another (Pichika et al., 2012). Novelty seeking and reward dependence was also found to not differ significantly between recovered BN and healthy controls (Pichika et al., 2012). In state anger scores, remitted BN patients showed healthy levels but greater discordance between both implicit and explicit anger and anxiety compared to controls (Tarrega et al., 2014). Concerning personality features, trait anger levels, in remitted BN EATING DISORDERS WILEY 767

patients were also not significantly different than those reported by controls which may suggest an improvement (Tarrega et al., 2014).

### 4.3 | Neurophysiological functioning

Improvements after treatment were reported in neurophysiological deficits present in the acute manifestation of the disorders in several studies. Long-term recovered AN patients regained subcortical gray matter volume (GMV) and global cortical thickness, not significantly differing from healthy controls (Friederich et al., 2012; King et al., 2015). Similarly, cortical thinning in acutely ill AN patients reversed shortly after beginning of therapy (Bernardoni et al., 2016). Such recovery of GMV areas and cortical thickness indicates possible reversibility and that such alterations may be disease state related and not a trait-like marker of EDs. However, GMV alterations were found to persist even after weight restoration or recovery and did not return to optimal healthy status in other studies. In remitted and long-term weight recovered AN patients, GMV of specific areas (anterior cingulate cortex and supplementary motor area) associated with perfectionism, cognitive behavioral flexibility, excessive error concerns, performance, planning, and motor control actions were found to be reduced compared to healthy controls (Friederich et al., 2012; Mühlau et al., 2007). This is consistent with reports from Joos et al. (2011), which found significantly less GMV in recovered AN patients compared to controls. Furthermore, the same recovered AN group did not significantly differ from acutely ill AN patients in GMV of the precuneus area only, associated with deficits in self-processing and episodic autobiographic memory retrieval. Remitted AN also showed increased GMV in the medial orbital frontal cortex indicating altered circuits in taste pleasantness (associated with stronger sensory experience of food stimuli, which could be experienced as overwhelming and led to avoidance), as well as reduced white matter in right temporal and parietal areas, indicating altered sensitivity to reward, when compared to healthy controls (Frank et al., 2013). AN patients even after successful weightrestoring treatment, exhibited over-responsiveness to sensory stimulation correlated with ED symptoms (Brand-Gothelf et al., 2016). Greater structural white matter connectivity that connects taste/reward processing regions was reported in another study, indicating a possible biological marker that alters the normal motivation to eat (Shott et al., 2016).

Other neurophysiological modifications may persist or emerge in AN. Recovered AN patients show a novel pattern of lower mean diffusivity which in fronto-parietal areas is associated with cognitive control and failure to disengage from a mistake (Yau et al., 2013). Another possible marker may be a distorted resting-state functional connectivity in the fronto-parietal network, compared to controls, associated with cognitive control (Boehm et al., 2016). Moreover, brain circuitry activation in response to hunger in recovered AN significantly differed from healthy controls, indicating altered reward salience circuitry, with healthy controls being faster in decision making in hunger states (Wierenga et al., 2015).

An absence of amygdala and hippocampus activation during nonconflict trials possibly suggests a compromised ability to process emotionally significant stimuli (Bang et al., 2016). Indeed, recovered AN-

restricting type showed higher concentrations of serotonin (5-HT) transporter tracker compared to recovered AN-binging-purging subtype, suggesting differences in emotion regulation difficulties and impulse control (Bailer et al., 2007). In another study regarding brain-derived neurotrophic factor plasma levels associated with psychiatric comorbidity and food intake regulation, AN weight-restored patients were not significantly different compared to a control group, suggesting that neurotrophin dysregulation does not appear to be a stable trait-related feature following weight restoration (Phillips et al., 2016).

Reduced cortical thickness was also reported in fully and partially remitted BN patients by Cyr et al. (2017), specifically in the right inferior frontal gyrus compared to healthy adolescents, possibly accounting for deficits in cognitive functions of learning, control, and reward. Moreover, remitted BN patients were found to exhibit neurobiological alterations in terms of neuroendocrine imbalances (diurnal hyposecretion of cortisol) thought to play an important role in signaling satiety and hunger (Birketvedt et al., 2006). Recovered BN patients also showed lowaccuracy scores on the heart beat perception task compared to healthy controls, suggesting significant deficits in interoceptive sensitivity, that is, in perceiving bodily cues (Klabunde, Acheson, Boutelle, Matthews, & Kaye, 2013). Furthermore, remitted BN patients, contrary to their healthy counterparts, showed reduced responsiveness to reward learning following catecholamine drug-induced reduction, indicating reduced reinforcement learning which may lead to an inability to modulate behavior by utilizing reinforcement history (Grob et al., 2012). A single study reported an altered brain response to taste solutions in remitted BN patients compared to controls (Ely et al., 2017), suggesting metabolic states may not modulate neural response to rewarding stimuli. Therefore, disinhibited eating could be attributable to a failure to devalue food reward when already fed and may account for an exaggerated response.

Remitted BN patients also showed altered serotonin (5-HT) function (Bailer et al., 2011; Pichika et al., 2012; Steiger et al., 2005), which is thought to interfere with mood and appetite regulation. Additionally, in remitted patients with BN, contrary to expectations of malnutrition and Zinc deficiency, higher serum zinc concentrations were reported compared to controls, possibly due to greater nutrient intake (Zepf et al., 2017).

### 4.4 | Cognitive functioning

Among ED patients in recovery, results indicated that two cognitive functioning aspects may be deficient: executive functions and emotion regulation processes. In terms of executive functions, AN patients in remission underperformed compared to healthy controls in tasks involving visual perception, decision making, memory, social cognition network, and in set shifting (Holliday, Tchanturia, Landau, Collier, & Treasure, 2005; Buehren et al., 2011; McAdams & Krawczyk, 2011: Danner et al., 2012; Heled, Hoofien, Bachner-Melman, Bachar, & Ebstein, 2014; Lindner et al., 2014; Talbot et al., 2015; Steward et al., 2016) or showed no significant change after recovery (Bodell et al., 2014; Nikendei et al., 2011). Moreover, specifically in decision making, partially remitted AN patients were impaired compared to healthy controls (Steward et al., 2016). However, recovered or fully remitted AN patients showed improvements in global integration skills (Harrison, Tchanturia, & Treasure, 2011), in gambling-based decision making (Steward et al., 2016), and had verbal memory skills associated with social functioning that did not significantly differ from healthy controls (Bentz et al., 2017). Compared to acutely ill patients, several improvements have been documented: weight-restored AN patients improved in slight starvation-induced memory deficits (Buehren et al., 2011). However, both ill and weight-restored AN engaged medial prefrontal cortex less than healthy controls for self-relevant cognitions (McAdams et al., 2016). Sustained weight-restored AN exhibited greater externalizing bias, differing significantly from both acute AN and newly weight-restored AN (Harper et al., 2017). Additionally, recovered AN patients showed superior detail processing skills compared to controls (Harrison, Tchanturia, & Treasure, 2011).

Difficulties in emotion regulation were present after treatment in both AN and BN. Although fully recovered ED patients experience significantly less negative urgency defined as acting impulsively to alleviate negative mood, compared to actively ill patients, partially recovered ED groups did not differ from ill patients (Bardone-Cone, Butler, Balk, & Koller, 2016). Such findings in difficulties in emotion regulation in other studies were found in terms of impulsivity and inability to accept emotions in weight-restored and recovered AN patients (Bang et al., 2016; Brockmeyer et al., 2012; Haynos et al., 2014) and in terms of increased explicit emotional expression of anxiety and anger in recovered BN patients (Tarrega et al., 2014) compared to healthy controls. In a couple studies, however, remitted BN patients were found to not differ significantly from healthy controls in mood stability and restricted emotional expression (Steiger et al., 2005), whereas recovered AN patients were found to have better emotional processing skills compared to acutely ill patients (Oldershaw et al., 2012).

#### 4.5 | Quality of life and positive mental health

In several studies, ED patients exhibited low levels of quality of life and impaired positive functioning after treatment. Treated ED patients who no longer met ED diagnosis reported significantly lower quality of life compared to individuals with no ED diagnosis in psychological, physical, cognitive, work, and school domains (Ackard, Richter, Egan, Engel, & Cronemeyer, 2014). Moreover, psychological well-being (Tomba et al., 2017) improved after treatment, but was compromised compared to healthy controls. In partially recovered AN patients, one study reported poorer quality of life compared to both fully recovered patients and healthy controls (Talbot et al., 2015). However, gains in positive active behaviors, specifically recreational seeking behaviors, were observed in recovered ED patients (Harrison, Treasure, & Smillie, 2011) as well as reduced loneliness in fully recovered ED patients (Harney et al., 2014).

In social functioning as well, recovered AN patients showed reduced capabilities in the realms of work, home, private leisure, and relationships compared to healthy controls (Harrison et al., 2014). Moreover, such patients showed greater interpersonal sensitivity (Holtkamp et al., 2005), social problem-solving difficulties, and lower positive problem orientation (McAdams & Krawczyk, 2011). Recovered AN patients do not significantly differ from controls in important elements of social functioning, in

terms of empathy, emotional recognition, or social conformity according to one study (Morris et al., 2013). Self-liking was found to not significantly differ between sustained weight-restored AN and acutely ill AN (Harper et al., 2017), whereas self-esteem was lower than healthy controls in both recovered AN (Brockmeyer et al., 2013) and BN patients (Daley et al., 2008).

## 5 | DISCUSSION

The main aim of the present work was to provide a quantitative metaanalytic synthesis to examine residual ED symptoms in ED patients. Findings of studies included in the meta-analysis mostly provided data on BMI and eating symptomatology comparisons of remitted or recovered AN patients with a control group measured with standardized psychometric instruments. The meta-analytic results, taken together, indicate that remitted and recovered AN patients report considerable residual core ED symptomatology in terms of greater ED-related symptoms and significantly lower BMI compared to healthy controls. Residual core ED symptoms measured with EDE-Q and EDI comprised dietary restraint, eating, weight, and shape concerns, drive for thinness, bulimic symptoms, and body dissatisfaction. Moderator analyses revealed that neither age nor study quality explains the observed differences between remitted and recovered AN patients and healthy controls in BMI or ED symptoms. Although a meta-analytic synthesis was not possible for studies on BN and BED, the data from the qualitative systematic review support nonetheless the presence of residual ED symptomatology in remitted and recovered BN as well.

The presence of residual core ED symptomatology in patients considered remitted or recovered, supported by both quantitative and qualitative syntheses, is concerning as they are known to be predictors of relapse of EDs (Richard et al., 2005; Vall & Wade, 2015). Other residual ED symptoms such as body-checking and body anxiety, food addiction behaviors, and food-related anxiety were also present, however, less is known about their predictive role in relapse (Levinson, Brosof, Ma, Fewell, & Lenze, 2017). It is plausible that core ED symptom occurrence might be related to several issues. In the selected studies, the treatment information was not sufficiently detailed and may not have been standardized and therefore not yet proven to be effective for EDs. Additionally, the inclusion of nutritional rehabilitation, recommended by clinical guidelines (Halmi, 2009: National Health Service, 2017), is not verifiable and often not mentioned. Several studies did not find differences in ED symptoms between remitted or recovered ED patients and healthy controls; however, this may have been due to a lack of statistical power and small sample sizes.

To examine whether the strictness of the applied remission and recovery criteria in the selected studies plays a role in the detection of residual ED symptoms, an additional moderator analysis was performed for AN patients in the meta-analyses. However, remission and recovery criteria strictness was not found to explain variations of results across studies on AN. Specifically BMI differences between remitted or recovered AN patients and controls did not depend on the type of remission criteria used (minimally, moderately, or strict criteria). It is noteworthy that despite the existence of recommended strict criteria, the majority of studies found in the literature did not use such definitions.

The second aim was to systematically review the literature on other non-ED clinical features in remitted and recovered EDs. The presence of comorbid psychiatric symptoms, general psychopathology, dysfunctional personality traits, neurophysiological alterations, cognitive deficits, as well as compromised quality of life and positive functioning in remitted and recovered ED patients is supported by the qualitative synthesis.

The literature suggests that the identified outcomes concerning these clinical features cannot be considered residual ED symptoms as they are not part of the illness per se, but may be premorbid, precede, or create vulnerability to eating psychopathology or be a consequence of the ED itself. Specifically, anxiety and depression were found to co-occur with residual ED symptoms. Both are frequently comorbid mood disturbances in EDs and are highly correlated with eating psychopathology (Godart, Flament, Perdereau, & Jeanmet, 2002; Godart et al., 2007; Mischoulon et al., 2011). Several clinical cognitive theories hypothesize an underlying role of mood disturbance in the development of EDs, suggesting that patients enact dysfunctional eating behaviors (e.g., binging purging and dietary restriction) and excessive exercise as a means to avoid or to cope with their negative emotions (Cooper, 2005; Fairburn, Cooper, & Shafran, 2003). Negative emotion states might create vulnerability to eating psychopathology (Deep, Nagy, Weltzin, Rao, & Kaye, 1995; Measelle, Stice, & Hogansen, 2006). Their presence is of clinical relevance as there is evidence that anxiety, mood alterations, and hopelessness may be associated with chronicity in EDs (Dawson, Rhodes, & Touyz, 2014; Nordbø et al., 2012; Robinson, Kukucska, Guidetti, & Leavey, 2015), with worse quality of life (Martin, Padierna, Lorono, Munoz, & Quintana, 2017), as well as with relapse of comorbid mood disorders (Mischoulon et al., 2011). Other authors have supported the notion that mood disturbance is a consequence of the ED, particularly of restrictive eating (Bergh et al., 2013; Gutierrez, 2013; Ioakimidis et al., 2011).

Similarly, the co-occurrence of dysfunctional personality traits, such as perfectionism and harm avoidance, further support the hypothesis that these might underlie the maintenance of ED symptoms (Cassin & von Ranson, 2005). The possible predisposing role of personality traits in ED development, in particular perfectionism in AN and impulsivity in BN, has been widely acknowledged. In addition, their presence before ED onset and their persistence after recovery have already been documented (Kaye, 2008; Wonderlich & Mitchell, 2001). Perfectionism and harm avoidance have been found to correlate with both worse ED psychopathology and comorbid psychiatric symptoms (Slof-Op't Landt, Claes, & van Furth, 2016). Additionally, schizotypal features and associated poor social functioning may have a longitudinal course, being present both in females with subclinical disordered eating behaviors (Raynal, Melioli, & Chabrol, 2016) as well as in females with chronic EDs (Larsson & Hellzen, 2004). Neuropsychological literature suggests that such personality characteristics, for example, perfectionism, may be the manifestation of underlying genetic and neuropsychological traits of cognitive inflexibility and hence of associated neurobiological alterations (Friederich & Herzog, 2011; Kaye, 2008). Several studies concerning psychiatric comorbidity and personality traits did not report differences in

such aspects in remitted or recovered ED patients compared to healthy controls; however, this may be due to a lack of statistical power.

Neurophysiological alterations and cognitive deficits are also found in remitted ED patients, in line with previous studies and reviews (Kaye, 2008; Friederich & Herzog, 2011; Kanakam & Treasure, 2013). However, such features may play both a predisposing role and represent vulnerability factors or be a consequence of the disorder. This has been suggested for brain volume deficits (Seitz et al., 2018), altered 5 HT function which regulates mood, social behavior, impulsivity, and eating behavior (Steiger & Bruce, 2007), set shifting, related to cognitive inflexibility, and emotional processing difficulties (Kanakam & Treasure, 2013; Kaye, 2008; Lavender et al., 2015; Mallorquí-Bagué et al., 2018; Sloan et al., 2017; Steiger & Bruce, 2007). Authors have indicated a possible neurobiological progression of EDs attributed to the effects of prolonged malnutrition in AN and of intermittent binge eating and restriction in BN (Treasure, Stein, & Maguire, 2015), suggesting to conceptualize EDs in more biologically based taxonomies (Kanakam & Treasure, 2013; Kaye, 2008). Such considerations are in line with findings indicating reversibility of GMV and cortical thickness loss in remitted AN, suggesting these be seen as disease state-related and not trait-like markers of EDs. However, other studies indicated a persistence of several brain alterations, for example, reduced white matter, which may be considered instead a biological marker for ED that alters eating patterns. A few studies on cognitive and neurophysiological functioning did not report differences between remitted or recovered ED patients compared to healthy controls, however, this may be due to small sample sizes which lack statistical power.

Finally, in several studies, remitted and recovered ED patients still exhibited compromised quality of life and positive functioning when compared to controls. Moreover, the lack of differences in a couple of studies on self-liking and social functioning between remitted or recovered patients and healthy controls may warrant larger studies to support such findings. Impairment in positive aspects, often neglected in research, is noteworthy as there is evidence that such deficits may be associated with chronicity or relapse in EDs (Espindola & Blay, 2009; Rodríguez-Cano, Beato-Fernandez, Moreno, & Vaz Leal, 2012) and in other psychiatric populations (Fava, 2012; Ryff, 2014). Indeed, recovered ED patients frequently express, as obstacles to their recovery process, a subjective sense of low empowerment, lack of autonomy, lack of supportive, meaningful, and healthy relationships, as well as a lack of self-acceptance (Espíndola & Blay, 2013; Tomba et al., 2017). Such paucity of well-being may be either premorbid to the disorder or a consequence of the ED and if not properly assessed and addressed might interfere with the recovery process (Tecuta & Tomba, 2018; Tomba et al., 2017).

## 5.1 | Implications for assessment of residual ED symptoms in remitted and recovered AN

The current work supports the need of refining the assessment of residual ED symptoms especially in AN. A possible solution in line with the medical model might reside in the application of a longitudinal conceptualization of the illness represented by the staging model, which underscores the transitional nature of psychiatric illnesses that can alternate between pathological and nonpathological statuses during the course of the disorder. As an important stage of transition from the acute stage to remission or recovery, the residual stage warrants clinical attention (McGorry et al., 2006) and should be considered an important clinical target to prevent relapses and chronicity (Cosci & Fava, 2013; McGorry et al., 2006). Clinical staging is both a model of clinical judgment and of assessment. Staging differs from, but may be complementary to, traditional forms of diagnosis such as those found in the Diagnostic and Statistical Manual for Mental Disorders (APA, 2013). It focuses on the extent and timing of progression of disease at a particular point in time, to better identify patients along the continuum of illness development, rather than on collections of cross-sectionally observed symptoms. A central intent of the staging model is the differentiation of early and milder clinical phenomena and identification of features of progression and chronicity, to guide the clinician in the selection of effective stageappropriate treatments.

Recent proposals for staging of AN (Cosci & Fava, 2013; Klein & Walsh, 2004; Maguire et al., 2008; Treasure et al., 2015) consider different longitudinal models of AN in terms of stage of severity (Maguire et al., 2017) or consider phases such as at-risk, early, middle (acute), and severe and enduring (chronic; Treasure et al., 2015) with corresponding suggestions for interventions. With the exception of one staging model for AN proposed by Cosci and Fava (2013), none identify a residual phase that may manifest or endure after acute phases. The current meta-analysis may be of support to better characterize and define the ED outcomes that warrant clinical attention in the residual phase of AN such as BMI, dietary restraint, eating, weight and shape concerns, drive for thinness, bulimic symptoms, and body dissatisfaction. The use of repeated assessments during the course of treatment that considers the identified residual ED symptoms in AN considered remitted or recovered is recommended.

## 5.2 | Implications of definitions of remission and recovery in EDs

Another possible implication which emerged from the current work is the need to systematically adopt a shared definition across ED outcomes and its measurement. Moreover, the data highlight the necessity to broaden the definitions of remission and recovery in EDs beyond ED symptomatology. Although not statistically significant, the differences between remitted and recovered AN patients and controls in BMI were larger and with higher variance in studies which used minimally strict remission criteria, suggesting that minimally strict criteria, based mostly on weight restoration, may capture only a part of the remission-recovery spectrum. Stricter criteria might be able to identify remitted or recovered AN patients who do not differ significantly from healthy controls, specifically in BMI. Future studies should further examine the relationship between residual symptomatology and the strictness of remission or recovery definitions, also in line with the literature which suggests the importance of using strict criteria to define remission and recovery in EDs (Ackard, Richter, Egan, & Cronemeyer, 2014; Bardone-Cone et al., 2010).

Furthermore, the current work highlights and supports the importance of using multicomponent strict criteria to define remission and recovery across EDs to better identify patients who, in achieving "recovery", are indeed more similar to healthy counterparts in various areas of functioning. Indeed, the recovery model (Andresen et al., 2011), which recently emerged to define recovery in psychiatry, underscores the importance of considering the personal experience of hope, connection, and establishing a personally fulfilling life, in accordance with similar recommendations (Ackard, Richter, Egan, Engel, & Cronemeyer, 2014; Tomba, Offidani, Tecuta, Schumann, & Ballardini, 2014; Fava & Bech, 2016; de Vos et al., 2017; Bardone-Cone et al., 2018). Moreover, in line with neuropsychological literature which underscores the importance of including neuropsychological tasks in treatment, for example, to improve set-shifting and cognitive flexibility (Vall & Wade, 2015), we suggest considering such areas of functioning in defining remission and recovery in EDs as well. Ensuring measurements of improvements in psychiatric comorbidity and personality traits in ED patients after treatment may assist in achieving a better definition of recovery, as such clinical aspects characterize remitted ED patients. Finally, objective measures might more accurately guide treatment selection and prognostic trajectories. Measurement need not be limited to psychometric tools for eating symptoms

and behaviors. A joint use of biological, neurophysiological, and psychometric tools (Fava, Rafanelli, & Tomba, 2012) may be reasonable and profitable in EDs as has been found in other psychiatric populations.

### 5.3 | Limitations

There are several limitations in the current work. While the current systematic review with meta-analysis is primarily based on the medical model, other innovative and emerging theoretical models might be considered. For example, the network analysis model may provide a powerful framework to study the interactions among the identified symptoms and clinical outcomes and their role in ED development and maintenance, as well as provide important insights in the definitions of residual symptomatology, remission, and recovery. Network analysis theory posits that mental disorders are characterized by interactions between different components (symptoms) which interact through direct causal relationships in a psychopathology network (Borsboom, 2017).

An additional limitation resides in the exclusion of other ED groups from the quantitative synthesis, in particular, BN and BED, due to a lack of sufficient data and the disparate use of measures and outcomes in the literature. Moreover, the application of a systematic review methodology which requires the identification of limited keywords and predetermined methods of data extraction may have limited the types and quality of studies that emerged in the literature search.

There are also several limitations of the cited primary studies. First, many of the studies were cross-sectional and observational in design. Most were nonexperimental, with weak to moderate quality. The fact that most studies were not intervention studies made three items from the checklist of quality assessment not applicable, thus lowering the quality rating (items on treatment description, follow-up, and attrition bias). Moreover, in studies concerning neurophysiological and cognitive functioning outcomes, the quality rating was penalized due to small sample sizes and due to a lack of description of the validity and reliability of physiological instruments and measures. Finally, several studies that were included did not detect differences between remitted and healthy controls or acutely ill patients, which may be due to lack of statistical power rather than to a lack of a difference of clinical significance.

## 6 | CONCLUSIONS

The current work highlights and supports the importance of systematically and consistently evaluating residual ED symptoms after treatment in AN. Future research may expand current findings on AN by using more strict criteria for recovery and evaluate if the identified residual ED symptoms, psychiatric comorbidity, neurophysiological and cognitive functioning, and quality of life differs in those more stringently recovered cases compared to healthy controls.

Research on remission and recovery in EDs may benefit from applying consistently and across studies stricter remission and recovery criteria across EDs (Bardone-Cone et al., 2018; Khalsa et al., 2017). In particular, residual symptoms in remitted or recovered BN patients should be further studied. Moreover, remission and recovery criteria should be more clearly defined for BN patients. Additionally, such studies may use standardized comparable outcomes to better define the residual ED symptoms that may be present in BN patients after treatment. With regards to BED, both definitions of remission and recovery and data on remitted patients are lacking and warrant extensive investigation.

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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