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REVIEW

The sequential approach in eating disorders: A scoping systematic review

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Abstract

Objective: The sequential model has been defined as an intensive, two-stage approach that comprises administering two types of treatment consecutively to improve treatment outcomes in cases of non-optimal or absence of treatment response. A psychiatric population that would potentially benefit from the application of the sequential model is the eating disorders (EDs) population. The current scoping review aimed to explore the emerging literature on the application of sequential treatments in EDs.

Method: Using PRISMA and Population intervention comparison outcomes study guidelines, Pubmed and PsycINFO were systematically searched for studies which applied temporally sequential treatments in patients diagnosed with EDs from inception to April 2022 using a combination of keywords. Studies utilising combined or integrated approaches were excluded.

Results: A total of 12 studies were selected and reviewed. Studies included Bulimia Nervosa, Binge Eating Disorder (BED), or mixed ED samples with a majority of female patients. No studies on AN samples were identified. The majority of studies contained a Cognitive-Behavioural Therapy module of treatment, were conducted on BED patients, were in outpatient settings, and included a group format in one or more treatment conditions. Studies varied in number of comparison groups and study design. Secondary and sequentially applied treatment modules were consistent with treatment recommendations of clinical guidelines.

Conclusions: The available data on sequential treatments in EDs is scarce and exhibits methodological limitations that should be addressed in future studies. Definition of sequential treatments in EDs should be further developed to guide robust clinical research and improve empirical support of sequential treatment for complex ED cases and for non-optimal ED treatment response.

KEYWORDS
eating disorders, sequential model, treatment

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Highlights

- Sequential treatments for eating disorders (EDs) have been applied exclusively in Bulimia Nervosa (BN), Binge Eating Disorder (BED) or mixed ED samples that are mostly female.
- Studies are heterogeneous in treatment paradigms, number of treatments applied, and comparison conditions, however, they are mostly psychological, based on Cognitive-Behavioural Therapy (CBT) or on behavioural interventions.
- To date, studies are limited and lack proper experimental design including appropriate control groups to determine the utility of sequential treatment versus single treatment.

1 | INTRODUCTION AND AIMS

The sequential model thus far has been defined in the psychiatric literature as an intensive, two-stage approach that comprises administering two types of treatment consecutively, including psychotherapy after pharmacotherapy, pharmacotherapy after psychotherapy, or sequentially applying two varying psychotherapeutic or pharmacological interventions. The model stems from the realization that a single course of a specific treatment (whether pharmacological or psychotherapeutic) rarely results in complete recovery either in research or clinical practice settings (Fava, 1999; Guidi & Fava, 2021) and that different intervention strategies may offer unique and independent contributions to a patient's well-being and to promote pervasive recovery (Fava, 1999).

Commonly used in clinical medicine, the application of treatments in sequential order occurs when the first treatment strategy fails or if response to treatment is deemed unsatisfactory or partial (Fava, 1999). Initially, in clinical psychiatry the application of treatments in sequential order had been limited mostly to treatment resistance and to pharmacological interventions, such as treatment-resistant depression (Borbély et al., 2022). In the past decades the combination of psychotherapy and pharmacotherapy has also become increasingly common, especially in mood disorders, with psychotherapy following pharmacotherapy being an effective treatment strategy for preventing relapse and recurrence (Guidi et al., 2011, 2016; Guidi & Fava, 2021). In anxiety disorders, the need to apply different psychotherapies consecutively and the importance of testing two approaches in controlled studies has been underscored for quite some time (Emmelkamp et al., 1993; Fava & Tomba, 2014).

Two are the main rationales for the application of the sequential model in clinical and psychiatric practice: (a) the persistence of residual symptoms after completion of either pharmacological or psychotherapeutic interventions despite successful response in the acute phase of the disorder, and (b) the frequent comorbidity with other disorders which negatively impacts both the longitudinal course of the illness and treatment outcomes, as in depression (Guidi & Fava, 2021), albeit the same can be said for psychiatric disorders in general.

A psychiatric population that, according to the rationales described above, could possibly benefit from the application of the sequential model is EDs. Eating disorders indeed are characterised by the persistence, even after completing standard treatment, of residual ED symptomatology and correlated psychopathological aspects, compromised social and cognitive functioning (Tomba et al., 2019) with subclinical presentations that persist decades after initial diagnosis (Stice et al., 2021). Furthermore, EDs present frequent common comorbidities with other psychiatric disorders (Godart et al., 2002, 2007).

Designing effective treatment interventions for EDs is thus particularly challenging, given their complex medical and psychological nature. Principal clinical practice guidelines recommend that treatments be personalised, offer care continuity and to not only aim for weight recovery, but rather encompass strategies that also improve important associated psychological and social factors (American Psychiatric Association, 2006, 2010; National Institute for Health and Care Excellence, 2020). In practice, the recommendations have contributed to the design of multicomponent treatments where specialised interdisciplinary teams offer a combination of psychotherapeutic, pharmacological, and nutritional support through individual, group, and family interventions, especially in the residential setting (Thompson-Brenner et al., 2019; Weltzin et al., 2014). The evaluation of outcomes in EDs has also become increasingly complex, with studies attempting to focus on the specific effects of psychological, pharmacological and nutritional interventions

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(Brauhardt et al., 2014; Davis & Attia, 2014) or attempting to focus on the treatment effects obtained in different treatment settings (Abbate-Daga et al., 2015; Brown et al., 2018; Friedman et al., 2016; Thompson-Brenner et al., 2019; Zanna et al., 2017) with medium to large effect sizes reported in clinical improvements.

So far, a few studies have underscored the impact such integrated treatments have on ED psychopathology and ED-related features and associated comorbid symptoms (Abbate-Daga et al., 2015; Grau Touriño et al., 2021; Zanna et al., 2017) as well as underscoring the lack of data on long-term efficacy especially for multidisciplinary residential treatment settings despite positive outcomes at end of treatment (Friedman et al., 2016).

Moreover, one critical issue that emerges with integrated treatment modalities is that little is known about the effects of the individual components or in what order or combination they best complement each other. Even less is known about the application and outcomes of sequential treatments in EDs. The advantages of applying multiple treatments sequentially rather than simultaneously lie in the possibility of differentiating their respective effects on patients and of making treatment more widely available and more cost effective in cases where only the patients that do not respond to a first attempt of treatment move incrementally to more intensive and costly therapies that also require more patient-therapist contact (Traviss-Turner et al., 2017). Standardized treatments for EDs may technically constitute a sequential approach as they are comprised of two treatment modalities that are applied in a temporally sequential manner. However, at the moment a consensus and definition of what constitutes sequential treatment in EDs is lacking as is lacking how standard treatment may be offered in a sequential manner to optimise treatment response. Moreover, a definition of treatment resistance in EDs and standardized treatment for treatment resistant cases, for which a sequential approach might be mostly beneficial, does not yet exist (Wonderlich et al., 2012).

While considering both advantages and drawbacks, the current systematic scoping review aimed to provide a first step in this research area by assessing the extent of the literature on the application of therapies and interventions in EDs that are explicitly defined by authors as sequential. A scoping review was deemed appropriate for studies which are heterogeneous in nature, making a conventional systematic review currently not possible (Peters, Godfrey, McInerney, et al., 2015). Deepening our knowledge on the sequential approach in EDs could help both researchers and clinicians to improve ED treatment outcomes.

1.1 | Aims of the review

The aim of the current review is to provide an overview of the existing ED research in which two or more treatment modalities have been applied sequentially, either explicitly defining the treatments as using a sequential approach or simply applying two temporally consecutive treatments. In this scoping review we used the definition of sequential treatment available in psychiatric literature (Fava, 1999; Guidi & Fava, 2021). In particular, the work aimed to answer the following questions:

1. What are the sample characteristics of these studies (age, gender, ED diagnostic groups, non-responders of previous treatments)?
2. What interventions have been applied sequentially and what interventions (if any) were they compared to?
3. What have these studies found in terms of reduced ED symptomatology or reduced ED-correlated symptomatology, effects on comorbidity, and drop-out rates after sequential treatments?

2 | METHOD

The present systematic scoping review has been conducted utilising the Joanna Briggs Institute scoping review protocol (Peters, Godfrey, McInerney, et al., 2015) as well as the Preferred Reporting Items for Systematic Reviews and Meta-analyses extension for scoping reviews guidelines (Tricco et al., 2018). The objectives, inclusion criteria, and methods for this scoping review were specified in advance (Peters, Godfrey, McInerney, et al., 2015).

2.1 | Search strategy

Pubmed and PsycINFO were systematically searched from inception to April 2022 utilising the following search terms: ("eating disorders" OR "anorexia" OR "bulimia" OR "binge eating disorder [ED]") AND "sequential" AND ("treatment" OR "approach" OR "intervention" OR "therapy"). The filter for "clinical trial" o "randomized controlled trial" was applied. Titles and abstracts were screened by two authors (L.T., E.T.) Articles that appeared potentially relevant were retrieved, and two reviewers (L.T. and E.T.) independently assessed the full reports, arriving at a consensus regarding eligibility. In case of disagreement, between the authors was dealt with by conducting multiple rounds of full-text revision, while discussions were carried out until

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consensus was reached with the aid of a research assistant (C.B.) if necessary. The review was supplemented by a manual search of the literature and references of selected studies. The study selection methodology is reported in the flow diagram (see Figure 1).

2.2 | Eligibility criteria

Eligible articles were in the English language and published in peer-reviewed journals. The Population Intervention Comparison Outcomes Study (PICOS) framework (Centre for Reviews and Dissemination, 2006) for eligibility criteria was used to identify inclusion and exclusion criteria. Studies were included if participants of the treatments were ED patients diagnosed with diagnostic manuals including the ICD-11 (World Health Organization, 2019) or previous versions and Diagnostic and Statistical Manual of Mental Disorders 5 or previous versions (APA, 2013). Studies were selected for inclusion if the treatment consisted of sequentially applied protocols or interventions either

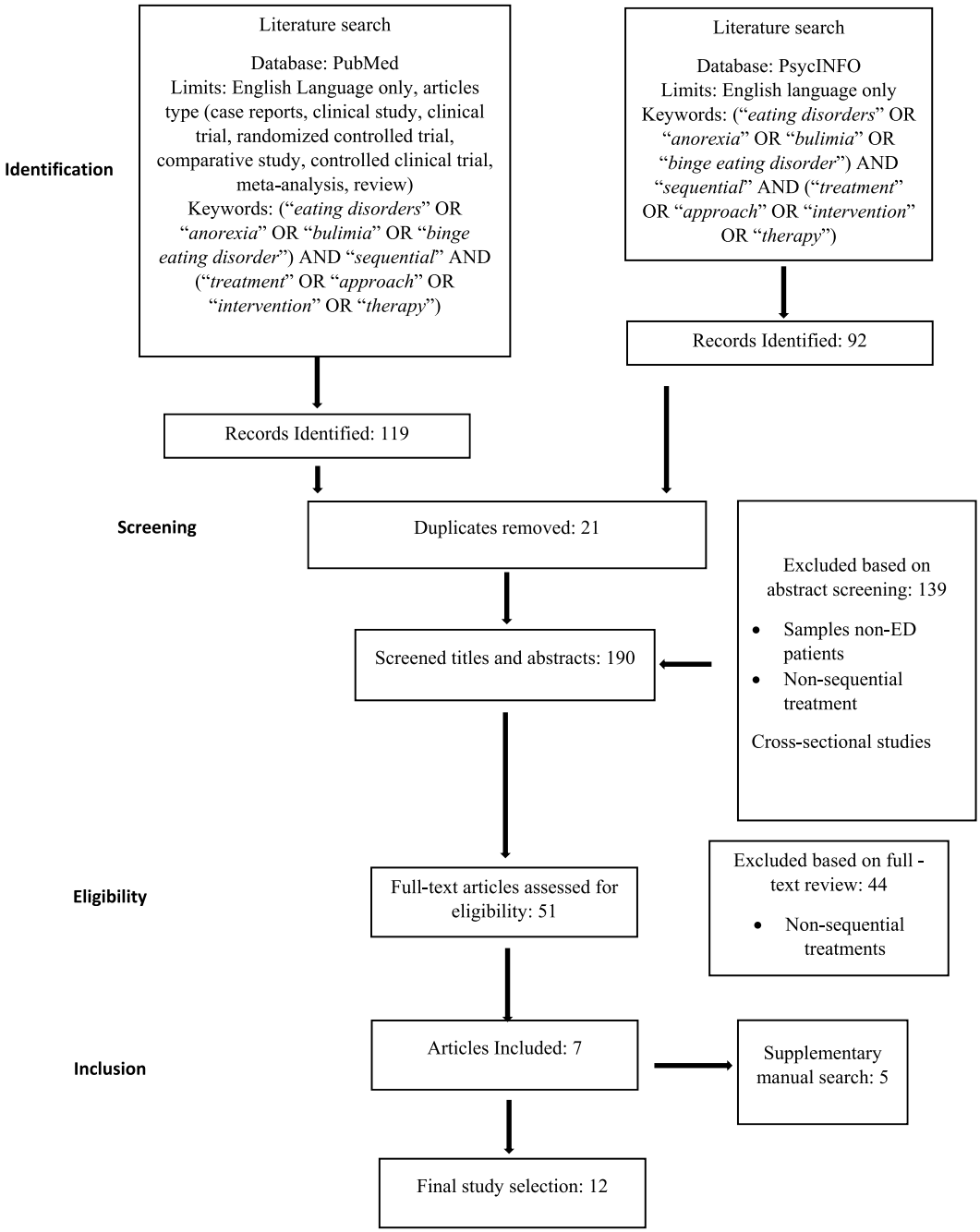

FIGURE 1 Flow Chart of the study selection process.

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psychological or medical treatments. Studies including standard treatment of EDs were also included when their sequential nature was underscored. Studies were included if they reported longitudinal data, as well as clearly stated the type of treatments applied. Moreover, they were included if studies reported at least one outcome, either in ED symptomatology or in other psychopathological symptoms or both. The following types of articles were included: case study, clinical study, clinical trial, clinical trial protocol, comparative study, controlled clinical trial, meta-analysis, randomized controlled trial, and reviews. Studies were excluded for the following reasons: they were cross-sectional, the sample was not composed of ED patients, studies did not report type of treatments applied and the effects of treatment on ED symptoms and/or other psychopathological symptoms, studies did not consist in sequentially applied treatments but of combined or simultaneously applied treatments. Please see Table 1.

2.3 | Data extraction

Data was extracted from papers included in the scoping review by the two authors (E.T. and L.T.) using the PICOS framework for data extraction (Centre for Reviews and Dissemination, 2006). The data extracted included specific details about the study, participants, methods, study design, study intervention, and key findings relevant to the review questions. Please see Table 1 for the extracted data. Any disagreements that arose between the authors was resolved through multiple rounds of full-text revision and discussions would be done until consensus was reached

TABLE 1 Population Intervention Comparison Outcomes Study (PICOS) criteria.

PICOS	Inclusion criteria	Exclusion criteria	Extracted data
Patients	• All ages • Female, male, or mixed gender studies • Patients with ED diagnoses (AN, BN, BED, OSFED)	Patients without ED	Study population: • Number of participants • Sex • Mean age • ED diagnoses • Presence of non-responders of previous treatments
Intervention	All types of psychological or medical interventions offered in a sequential treatment or approach	All types of psychological or medical interventions combined or simultaneous treatments	• Types of treatments or interventions • Length of treatments • Assessment times
Control group	Studies with or without a comparison group	None	• Control group characteristics • Group differences
Outcome	• Effects of treatment on ED symptoms • Effects of treatment on other reported psychopathological symptoms, comorbidity	None	• Measures used to assess ED symptomatology • ED symptoms • Other psychopathological symptoms or comorbidities • Changes over time due to treatment • Group differences • Drop-out rates and differences in drop-out rates
Study design	Longitudinal	Cross-sectional	• Type of study: Case study, clinical study, clinical trial, clinical trial protocol, comparative study, controlled clinical trial, meta-analysis, randomized controlled trial, and reviews. • Follow-ups • Assessment times • Study setting (outpatient vs. inpatient) • Treatment format (group vs. individual)

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with the involvement of a research assistant (C.B.) if necessary. If needed, authors of papers were contacted to request missing or additional data, where required.

3 | RESULTS

3.1 | Selection of articles

The search in Pubmed yielded 119 results, while the same search strategy yielded 92 results in PsycINFO. After eliminating duplicates ($n = 21$), 190 records remained. The screening of titles and abstracts led to the exclusion of 139 articles. Full-text review of the resulting articles ($n = 51$) led to the exclusion of further 44 additional articles and a total of seven studies were identified for inclusion in the review. Five additional studies were included through a manual search (See flow chart in Figure 1) for a total of 12 selected studies (information on selected studies are presented in Table 2).

3.2 | Study sample characteristics

With regards to study characteristics, many samples ($n = 10$; 83.3%) of the studies were with either exclusively female participants ($n = 5$) (Agras et al., 1994, 1997; Dean et al., 2008; Mitchell et al., 2002; Treasure et al., 1999) or with a majority of female participants ($n = 5$) (Agras et al., 1995; Grilo et al., 2011; MacDonald et al., 2021; Neveu et al., 2016; Tasca et al., 2018). Two studies (16.7%) did not report information of gender of participants (Allen et al., 2012; Treasure et al., 1996). The age of participants was between 18 and 65 years of age, thus containing adult samples. Sample sizes ranged from 15 (Neveu et al., 2016) to a maximum of 221 participants (MacDonald et al., 2021).

In terms of ED diagnoses, eight out of the 12 selected studies (66.7%) focused exclusively on a single diagnostic group while four studies (33.3%) examined mixed ED samples (Allen et al., 2012; Dean et al., 2008; MacDonald et al., 2021; Neveu et al., 2016). Among the studies on single diagnostic groups, more than half ($n = 5$, 62.5%) investigated BED patients (Agras et al., 1994, 1995, 1997; Grilo et al., 2011; Tasca et al., 2018) and a third ($n = 3$, 37.5%) investigated BN patients (Mitchell et al., 2002; Treasure et al., 1996, 1999). No study focused exclusively on AN patients. Three out of the 12 studies (25%) explicitly stated that participants were non-responders to a previous treatment (Agras et al., 1995; Mitchell et al., 2002; Neveu et al., 2016) while none of the selected studies were concerned with the treatment of comorbid conditions in ED patients.

3.3 | Study design characteristics

The clinical settings and experimental design of treatment implementation varied widely across studies. In terms of clinical settings, nine studies (75%) were in outpatient settings while the remaining three studies (25%) were conducted in intensive inpatient settings (MacDonald et al., 2021; Neveu et al., 2016) or inpatient setting (Dean et al., 2008).

Most studies, ($n = 9$, 75%) included group treatment modalities either in outpatient settings (Agras et al., 1994, 1995,1997; Grilo et al., 2011; MacDonald et al., 2021; Tasca et al., 2018; Treasure et al., 1999) or in inpatient treatment (Dean et al., 2008; Neveu et al., 2016). The remaining three studies (25%) exclusively tested therapies delivered in individual format in all treatment modalities offered (Allen et al., 2012; Mitchell et al., 2002; Treasure et al., 1996).

In terms of study design, all were longitudinal as per inclusion criteria with varying follow-up time frames spanning from a minimum of 10 weeks (Allen et al., 2012) to a maximum of 26 months (Treasure et al., 1996). Eight studies (66.7%) included intermediate assessment points and 10 studies (83.3%) included one or more follow-ups, while the remaining two only reported pre-post-measurements (see Table 2 for details).

Most studies had a control or comparison group ($n = 10$, 83.3% of all reviewed studies). Three out of the 10 studies with comparison groups (30%) compared one single treatment to two sequentially applied treatments (Allen et al., 2012; Tasca et al., 2018; Treasure et al., 1996), while seven studies (70%) examined and compared multiple sequential treatments (two or more) (Agras et al., 1994, 1995; Dean et al., 2008; Grilo et al., 2011; MacDonald et al., 2021; Mitchell et al., 2002; Treasure et al., 1999). Two studies examined two sequentially applied interventions (Agras et al., 1997; Neveu et al., 2016) without a comparison group (see Table 2 for details).

3.4 | Type of interventions

In terms of theoretical paradigms used in the outpatient and inpatient interventions, most studies ($n = 11$, 91.6%) consisted in psychotherapeutic treatments in particular cognitive behavioral therapy (CBT) (Agras et al., 1994, 1995, 1997, Grilo et al., 2011; MacDonald et a., 2011; Mitchell et al., 2002; Treasure et al., 1996) or CBT-Enhanced (CBT-E) (Allen et al., 2012; Neveu et al., 2016) components or contained self-help modules which are also based on CBT ingredients (Tasca et al., 2018; Treasure et al., 1996).

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TABLE 2 Characteristics and relevant outcomes of selected studies.

Authors	Age (M±SD or range in years) Female (%) and diagnoses (N)	Non-responders to previous treatment (Yes/No)	Type of treatment groups and assessment time	Outcome Measures	Outcome: Changes over time	Outcome: Comparisons between groups	Outcome: Drop-out data
Agras et al., 1994	45 ± 10	No	Group BWL versus CBT + group BWL versus CBT + group BWL/D	-Binge-eating frequency	All groups demonstrated a significant reduction ($p < 0.02$) in the frequency of binge eating from the 36-week to the 52-week	No significant differences were found between the groups for either depression, or for dietary restraint.	Drop-out did not significantly differ during the 36 week-period between groups (27% in BWL, 17% in CBT + BWL, 23% in CBT + BWL/D)
			Assessment times: Baseline, 12–24 and 36 weeks (posttreatment), at 3 months follow-up	-Weight BDI, TFEQ	assessment period, WL (2.0 binge days/week, 14% abstinent), CBT/WL (1.7 binge days/week, 28% abstinent), and CBT/WL-D (1.5 binge days/week, 32% abstinent).	At 12 weeks: CBT superior to BWL for binge eating reduction ($p < 0.01$), but BWL superior to CBT for % weight ($p < 0.002$).	
	100%					At 24 weeks: D superior to BWL in disinhibition ($p < 0.008$).	
	BED (108)					At 36 weeks, differences in % of binge-eating abstinence and weight loss non-significant between groups.	
						No differences at follow-up in % weight loss, but the CBT + BWL/D group lost more weight than CBT + BWL ($p < 0.05$).	
Agras et al., 1995	47.6 ± 10.1	Yes	Assessment only ($n = 11$) versus Group CBT + BWL treatment (CBT responders) versus Group CBT + group IPT (CBT non-responders)	Frequencies of binge eating episodes	CBT associated with weight reduction ($p = 0.02$), in binges ($p = 0.0001$) in disinhibition ($p = 0.004$) and in BES ($p = 0.0001$).	Participants receiving treatment improved in weight ($p = 0.02$), binge-eating ($p = 0.0001$), BES ($p = 0.0001$) and disinhibition ($p = 0.004$) compared to the assessment only group.	During the 24-week treatment period, 14.3% dropped out of the treatment group, whereas 9.0% dropped out of the waiting-list control group.
	94%		Assessment: Pretreatment, post CBT at 12 weeks and post IPT at 24 weeks	Weight BDI, TFEQ, BES, IIP, SCL-90, Rosenberg self-esteem scale	BWL associated with significant change ($p = 0.0001$), with a decrease in weight of 4.1 kg ($p = 0.0001$), binge eating remained stable at a low level of 0.3 days/week	No differences in primary (binge-eating and weight) or secondary outcomes (remaining questionnaires) were found between the CBT-WL and CBT-IPT groups.	
	BED (50)				Group IPT associated with increased binge eating (+0.5 days/week) and weight (+0.6 kg), although the changes were not significant and no significant further gains in other measures.		

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TABLE 2 (Continued)

Authors	Age (M±SD or range in years) Female (%) and diagnoses (N)	Non-responders to previous treatment (Yes/No)	Type of treatment groups and assessment time	Outcome Measures	Outcome: Changes over time	Outcome: Comparisons between groups	Outcome: Drop-out data
Agras et al., 1997	46 ± 10.2 100% BED (93)	No	Group CBT + group BWL Assessment: At post CBT at 12 weeks, post BWL at 36 weeks, follow-ups at 52-70-88 weeks	BES, TFEQ, BDI, IIP	At the final follow-up assessment binge eating was reduced by 64% and 33% ($n = 25$) of participants were abstinent but weight loss was not maintained.	No comparison group available.	17 out of 75 (22.6%) dropped out of treatment at 1-year follow-up.
Allen et al., 2012	26.52 (MFT + CBT-E)/ 26.44 (CBT-E) ± 8.98	No	MFT + individual CBT-E versus Individual CBT-E only	EDE-Q, EDE, DASS, RMI	Significant main effects of time (pretreatment to post-treatment) were identified for Global EDE-Q scores, $p = 0.002$, binge eating, $p = 0.008$, and purging, $p = 0.001$, but not on BMI.	No significant interaction effects between time and treatment condition for any of the dependent variables, degree of symptom change over treatment did not differ significantly across the two groups.	Drop-out rates did not differ significantly between groups (55.8% in MFT + CBT-E vs. 53.5% in CBT-E) at post-treatment.
	- AN (21) BN (31) EDNOS: AN-like (34), BN-like (6), purging disorder (2), Unspecified (1)		Assessment: At pretreatment, at 5 and 10 weeks, at post-treatment		The MFT-CBT-E was associated with significant increases in readiness to change ($p > 0.01$)	No significant between-groups differences in treatment completion rates. At post-treatment, no significant differences between treatment conditions in full or partial remission from their eating disorder.	
Dean et al., 2008	22.4 ± 7.37 100% AN-R (15) AN-BP (6) BN (1) EDNOS (20): BN-like (17) AN-like (3)	No	Group MET + inpatient TAU versus Inpatient TAU only Assessment: At pre-treatment, pos-treatment and at the 6-week follow-up	ANSOCQ, DB, SES, Treatment engagement questionnaire, EDI-2, EDE-Q, BDI-II	For the initially underweight patients, no significant results in BMI. MET associated with higher completion rate ($p = 0.012$). Between post-treatment and follow-up assessments, TAU associated with greater reduction in functional avoidance ($p = 0.022$). Although the two groups did not differ across the course of the three assessment periods.	No single treatment available. No significant differences on any assessment measure, but TAU group reported a greater reduction on the EDI-2- drive for thinness at post-treatment ($p = 0.041$). Improvements in motivational measure in both groups, but between post-treatment and follow-up TAU associated with a reduction, while MET group reported increasing levels of motivation.	Drop-out rates did not differ significantly between treatment groups at post-treatment or follow-up (percentages not reported).

(Continues)

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TABLE 2 (Continued)

Authors	Age (M±SD or range in years) Female (%) and diagnoses (N)	Non-responders to previous treatment (Yes/No)	Type of treatment groups and assessment time	Outcome Measures	Outcome: Changes over time	Outcome: Comparisons between groups	Outcome: Drop-out data
Grilo et al., 2011	44.8 ± 9.4	No	Group CBT versus Group BWL versus Group CBT+Group BWL	SCID I, Structured clinical interview for DSM-IV axis I disorders, EDE, BDI-21	For the CBT + BWL group, non-significant changes during CBT for percent BMI loss weight and absolute weight loss.	No significant difference between treatments in frequency of binge eating at post-treatment in remission rates from BED at post-treatment, at 6-month and 12-month follow-up, in weight and BMI loss at 12-month follow-up.	Drop-out rates, which did not differ statistically, were 24% for CBT, 31% for BWL, and 40% for CBT- BWL at post-treatment.
	66% BED (125)		Assessment: At pre-treatment, every 2 months of treatment, at post-treatment and at 6 and 12 months follow-up		Significant changes during BWL for percent BMI loss ($p = 0.02$), weight ($p = 0.01$) and absolute weight loss ($p = 0.02$).	Differences between treatments in binge frequency, significantly lower in CBT than BWL at 6-month ($p = 0.009$) and 12-month follow-up ($p = 0.01$).	
MacDonald et al., 2021	28.4 ± 9.2 (IOP)	No	Intensive inpatient/day hospital treatment + IOP versus Intensive inpatient/day hospital treatment + individual CBT	EDE	Changes in the weight and shape concerns not significant at 6-month follow-up, but significant at 12-month follow-up ($p = 0.01$).	No single treatment available.	No drop-out data available.
	28.6 ± 8.6 (CBT) 97.1 (IOP) 94.1 (CBT) AN-R (20) AN-BP (22) BN (144) PD (35)		Assessment: At pre-treatment, after the intensive treatment, at post-treatment and at 6 and 12 months of follow-up			No difference between IOP group and individual CBT maintenance treatment in trajectory of return to clinically significant symptoms. Treatment type did not predict changes in weight/shape concerns between end-of-inpatient or day treatment) and 6- or 12-month follow-up.	
Mitchell et al., 2002	28 ± 7.3 (IPT)	Yes	CBT*+IPT versus CBT*+MED (fluoxetine/desipramine)	EDE, computerised interviews, TFEQ, Bulimic thoughts questionnaire, SCID I and II, BDI, Rosenberg self-esteem questionnaire, IIP, Weissman assessment of social adjustment scale, MPQ	37 CBT non-responders assigned to secondary sequential treatment completed treatment, while 25 dropped out or withdrew.	No single treatment available.	Drop-out rates did not differ significantly between groups (32% in IPT vs. 48% in MED) at post-treatment.
	27.1 ± 6.3 (MED)		Assessment: At pre-treatment and every 2 weeks up to week 34 (post-treatment) with 60-week follow-up		High dropout rates and low response rates were found in patients assigned to secondary treatments.	No significant differences were found between treatment groups in intent-to-treat analyses or completer analyses.	
	100% BN (62) Non-responders to 16 weeks -CBT)		*Not specified if group or individual format		No changes over time in psychometric measures available.	Abstinence rates did not differ significantly between groups.	

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TABLE 2 (Continued)

Authors	Age (M±SD or range in years) Female (%) and diagnoses (N)	Non-responders to previous treatment (Yes/No)	Type of treatment groups and assessment time	Outcome Measures	Outcome: Changes over time	Outcome: Comparisons between groups	Outcome: Drop-out data
Neveu et al., 2016	15 93% AN (6) BN (8) BED (1) Non-responders to 4 weeks of intensive CBT	Yes	Intensive inpatient with individual CBT-E and SSRI and multi-faceted therapeutic group programme + SB Assessment: At pre-treatment and after 16 and follow-up at 47 ± 7 weeks after discharge	Standardized self-administered questionnaire built for the purpose of the study, notebook	SB associated with a 44% relative reduction in the planned food intake ($p < 0.001$), a longer consecutive binge refractory period compared to regular binges ($p = 0.002$) and a reduction by 26% of binge number the day after each SB ($p = 0.004$). 47% of patients reached binge abstinence for four consecutive weeks 16 weeks after the first SB.	No single treatment available. No comparison group available.	2 out of 15 patients (13.3%) dropped out of the treatment condition.
Tasca et al., 2018	41.87 ± 12.73 (USH) 42.98 ± 12.80 (control) 44.97 ± 12.70 (GPIP) 88.9% (USH) 87% (control group) 84.6% (GPIP) BED (135)	No	USH + GPIP versus USH + no treatment Assessment: At pre-treatment, after 10 weeks and at week 2-9-14 of the group therapy, at 3 and 6 months of follow-up	SCID I, EDE, CES-D, IIP64, ECR, EDE-Q, TRIPED	Significant decline in the binge eating episodes in 28 days (13.30 vs. 5.99) ($p < 0.001$) and in EDEQ global scores ($p < 0.001$) after USH (15.5% of participants abstinent). Decline in interpersonal problems ($p = 0.004$) and attachment avoidance ($p = 0.009$) within the GPIP condition.	No single treatment available. No significant difference between GPIP and control groups in the reduction of binge episodes and depression. No difference between GPIP and control group in abstinence from BED after 6 months.	9 out of 39 (23.1%) dropped out of the treatment condition.
Treasure et al., 1996	25.6 ± 5.5 (manual + CBT) 25.9 ± 6.3 (CBT) – BN/BN-like (110)	No	Self-care manual + CBT* (8 sessions) versus Full course CBT* (16 sessions) Assessment: At pre-treatment, at 8 and 16 weeks and at 14–26 months of follow-up *Not specified if group or individual format	Investigator-based rating scale, SCID, BITE	Bulimic symptoms improved significantly in both groups ($p < 0.001$). At end of treatment 30% of the sequential group and 30% of the full course of CBT group were free from all bulimic symptoms.	No significant differences between the two groups on any of the measures at the end of treatment or at 18 months follow-up.	Drop-out rates did not differ significantly between treatment groups (27% in full-course CBT vs. 16% in sequential group) at post-treatment.

(Continues)

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TABLE 2 (Continued)

Authors	Age (M±SD or range in years) Female (%) and diagnoses (N)	Non-responders to previous treatment (Yes/No)	Type of treatment groups and assessment time	Outcome Measures	Outcome: Changes over time	Outcome: Comparisons between groups	Outcome: Drop-out data
Treasure et al., 1999	28.8 ± 7.8 (MET) 28.5 ± 7.2 (CBT) 100% BN (125)	No	Individual MET + group CBT Vs Individual CBT + group CBT versus Individual MET + individual CBT Assessment: At pre-treatment, at 4 and 12 weeks, at monthly follow-ups	Scale developed for European-wide COST action B6 project, URICA, WAI	Precontemplation and contemplation scores reduced marginally ($p < 0.06$) while action scores increased significantly ($p < 0.01$) with MET.	No single treatment available. Clinically significant improvements in binge frequency, vomiting frequency, and frequency of laxative use did not differ between treatment conditions.	Drop-out rates did not differ significantly between treatment groups (33% in MET groups vs. 24% CBT patient group) at post-treatment

Abbreviations: AN, Anorexia Nervosa; ANSOCQ, Anorexia nervosa stages of change questionnaire; BED, Binge Eating Disorder; BES, Binge Eating Scale; BDI, Beck Depression Inventory; BITE, Bulimia Investigation Test Edinburgh; BN, Bulimia Nervosa; BWL, Behavioural Weight Loss; CBT, Cognitive-Behavioural Therapy; CBT-E, Cognitive-Behavioural Therapy-enhanced; CES-D, Centre of Epidemiologic Studies Depression Scale; D, desipramine; DASS, Depression Anxiety and Stress Scale; DB, Decisional balance for anorexia; DSM, diagnostic and statistical manual of mental disorders; ECR, Experiences in Close Relationships Scale; EDI, Eating Disorders Inventory; EDNOS, Eating Disorder not otherwise specified; GPIP, group psychodynamic interpersonal psychotherapy; IIP, Inventory of Interpersonal Problems; IOP, group-based intensive outpatient programme; IPT, Interpersonal Therapy; MED, medication therapy; MET, Motivation Enhancement Therapy; MFT, Motivation-Focused Therapy; MPQ, Multidimensional Personality Questionnaire; OQ, Outcome Questionnaire; PD, Purging Disorder; RMI, Readiness and Motivation Interview; SB, Sequential Binge; SCID, Structured Clinical Interview for DSM-IV-TR Disorders; SCL-90, Symptom Check List-90; SES, Self efficacy scale for anorexia nervosa; TAU, Treatment as usual; TFEQ, Three-Factor Eating Questionnaire; TRIPED, Tape Rating Instrument for Psychotherapy of Eating Disorders; URICA, 24-item University of Rhode Island Change Assessment Scale; USH, unguided self-help; WAI, Working Alliance Inventory; WL, Weight Loss.

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Three studies examined the sequential combination of two psychological interventions such as CBT and behavioural weight loss (BWL) programs (Agras et al., 1995, 1997; Grilo et al., 2011). Two studies sequentially added motivational-type therapies to CBT therapies (Allen et a., 2011; Treasure et al., 1999), three sequentially added interpersonal therapy to CBT (Agras et al., 1995; Mitchell et al., 2002; Tasca et al., 2018).

In two studies psychological treatments were offered following intensive programs which included inpatient and day hospital programs. In particular in MacDonald et al. (2021) individual CBT and an intensive outpatient group treatment, which also contained a CBT element, were compared as maintenance regimes after intensive treatments. In Dean et al. (2008) Motivational Enhancement Therapy (MET) before a treatment as usual (TAU) inpatient programme (that was not defined) was compared to TAU inpatient programme alone.

Two studies utilised pharmacological treatment (Agras et al., 1994; Mitchell et al., 2002) after CBT. Specifically, fluoxetine a selective serotonin reuptake inhibitor (SSRI) was administered to still-symptomatic patients after CBT in Mitchell et al. (2002) while desipramine (a tricyclic antidepressant) was used in Agras et al. (1994) simultaneously with BWL and after a first phase of CBT. In another study (Neveu et al., 2016), a SSRI (not specified) was part of an intensive inpatient CBT-E based treatment which was followed by a novel behavioural intervention called "sequential binge".

3.5 | Sequential treatments in Bulimia Nervosa patients

Three studies (25%) looked at sequential treatments in BN patients or with BN-like symptoms (Mitchell et al., 2002; Treasure et al., 1996, 1999) focussing on the sequential administration of psychological and/or pharmacological treatments to CBT. The sequential addition of Interpersonal Therapy (IPT) for BN (Fairburn, 1993; Klerman et al., 1984) or fluoxetine (followed by desipramine in case of non-improvement) following CBT for BN (Fairburn et al., 1991) in non-responders (Mitchell et al., 2002) did not result, albeit the sequential treatments were not compared to single treatments, in improving abstinence rates from binging for either treatment group of treatment completers (24% in IPT and 19% in medication groups). In another study (Treasure et al., 1996), comparing a psychological treatment consisting in a full 16-session course of CBT for BN (Fairburn et al., 1991) to two psychological treatments consisting of eight sessions of a CBT-based self-help manual for BN (Schmidt & Treasure, 1993) sequentially followed by only eight sessions of CBT for BN (Fairburn et al., 1991), found significant improvements in bulimic symptoms in both groups with no significant differences between the two treatment groups on any of the bulimic symptoms measures at the end of treatment or at 18 months of follow-up. At end of treatment, 30% of patients in the sequential group and 30% in the standard CBT treatment group were free from all bulimic symptoms (Treasure et al., 1996). In the remaining study (Treasure et al., 1999) comparing three groups in which two psychological treatments were offered in sequential order, MET followed by group CBT, MET followed by individual CBT, and individual CBT followed by group CBT, clinically significant improvements observed in binge frequency, vomiting frequency and frequency of use of laxatives did not differ between treatment conditions, albeit the sequential treatments were not compared to single treatments. The MET approach was adapted for EDs and added to a manual for the treatment of BN (Schmidt & Treasure, 1997). No significant differences in drop-out rates were found between treatment conditions in all three studies (Mitchell et al., 2002; Treasure et al., 1996, 1999).

3.6 | Sequential treatment in binge eating disorder patients

Five studies focused on sequential treatment in BED (Agras et al., 1994, 1995, 1997; Grilo et al., 2011; Tasca et al., 2018), mostly consisting in the sequential administration of psychotherapeutic treatments (Agras et al., 1995, 1997; Grilo et al., 2011; Tasca et al., 2018), while one contained a pharmacological treatment as well (Agras et al., 1994).

Four (80%) of the five studies on BED patients examined BWL programs using a specific manualized intervention aimed at weight loss (WL) proposed by Brownell (1985, 2000) that follows the LEARN (Lifestyle, Exercise, Attitudes, Relationships, Nutrition) model for weight management. The programme was tested sequentially after CBT in these studies (Agras et al., 1994, 1995, 1997; Grilo et al., 2011).

In particular, Agras et al. (1994) examined the differences between three randomized treatment conditions consisting in BWL alone, the sequential addition of CBT to BWL, the sequential addition of CBT to BWL combined with pharmacotherapy (desipramine). At 12 weeks, the BWL + CBT condition was found to be superior to the BWL only condition for binge eating reduction, but the BWL only condition was superior to BWL + CBT for percentage weight change. Instead at 24 weeks, the groups receiving desipramine with BWL after CBT had

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superior results in disinhibition compared to BWL treatment alone. However, at both end of treatment and follow-up, no differences between the treatment groups were reported in percentage WL or percentage of reduction in days of engaging in binge-eating. No single treatment was present as a comparison group.

Similarly, in Grilo et al. (2011)'s study, the sequential administration of BWL following CBT (CBT + BWL) was compared to CBT and BWL alone. Cognitive-behavioural therapy was superior to BWL for reductions in binge-eating at 6-month and 12-month follow-ups, while BWL produced statistically greater, albeit modest, weight losses during treatment (Grilo et al., 2011). However, the three treatments, CBT alone, BWL alone, and CBT + BWL, did not differ significantly in their effects on associated ED psychopathology, depression, and remission from binge-eating at post treatment, 6-month and 12-month follow-ups, thus not supporting the utility of the sequential approach of providing BWL after CBT but rather, according to authors, supporting the notion of offering BWL as an alternative to CBT when CBT is unavailable to BED patients.

In Agras et al. (1995), BWL, offered to CBT responders after a first phase of group CBT, was compared to group IPT offered after a first phase of group CBT to CBT non-responders. No differences in primary or secondary outcomes were found between the two different psychological sequential treatments of group CBT-BWL and group CBT-IPT groups (Agras et al., 1995). Additionally, adding group IPT to group CBT for non-responders of CBT was associated with increased binge eating (+0.5 days/week) and weight (+0.6 kg) although these changes were not statistically significant. The follow-up study (Agras et al., 1997) of the CBT + BWL group revealed that binge eating frequency and binge-eating abstinence was further improved as were other measures of interpersonal problems, depression symptoms, hunger and disinhibition. The lack of a treatment comparison group doesn't allow any conclusions to be drawn concerning the benefit of the administration of sequential treatments of two psychological interventions versus single treatments or regarding differential effects of sequential treatments.

The remaining study on BED patients (Tasca et al., 2018) focused on comparing two psychological treatments, in particular unguided self-help manual (USH) followed by group psychodynamic-interpersonal psychotherapy (GPIP), and USH followed by a no treatment condition, thus essentially USH only. The USH manual is based on a 10-week individual CBT-oriented Unguided Self-Help programme described in the book by Fairburn (2013). The sequential addition of GPIP after USH did not contribute to any further reductions in frequency of binge-eating compared to undergoing USH followed by no treatment, the control condition, but did result in significant and large improvements in both attachment avoidance and interpersonal problems.

In terms of drop-out differences between treatment conditions, drop-out rates did not significantly differ between treatment groups in Agras et al. (1994) (27% in BWL, 17% in CBT + BWL, 23% in CBT + BWL with Desipramine). The sequential treatment approach of CBT + BWL in Grilo et al. (2011) also did not differ significantly compared to when the treatment modules were tested individually. In Agras et al. (1995) 14.3% dropped out of the treatment group, whereas 9.0% dropped out of the waiting list control group but it is unclear whether this difference was significant. In the 1-year follow up, 22.6% dropped out of treatment (Agras et al., 1997). In the sequential treatment condition comprise of USH and GPIP 23.1% of participants dropped out (Tasca et al., 2018).

3.7 | Sequential treatments in mixed eating disorder samples

Four studies (33.3%) examined sequential treatments in mixed ED groups (Allen et al., 2012; Dean et al., 2008; MacDonald et al., 2021; Neveu et al., 2016), mostly consisting in the sequential administration of psychotherapeutic treatments before and after intensive treatment protocols. Such intensive protocols were described as highly structured inpatient or outpatient/day hospital treatments. Two intensive hospital-based treatments included CBT and some kind of meal support or nutritional component of treatment (MacDonald et al., 2021; Neveu et al., 2016) while one is not described (Dean et al., 2008).

In one study, a psychotherapeutic intervention, MET, preceded the intensive hospital programme, and comprised a brief group-based inpatient programme to prepare and motivate for intensive treatment (Dean et al., 2008). In another study individual CBT followed, as a maintenance treatment, the intensive hospital programme (MacDonald et al., 2021), while in another study, a behavioural intervention (called "sequential binge" or "SB") followed inpatient treatment for poor responders of the intensive hospital treatment (poor response was defined as poor reduction in binging frequency over the past 4 weeks, with mean reduction between 6% and 27%) (Neveu et al., 2016). Only one study on sequential treatment in mixed ED (Allen et al., 2021) assessed the effects of applying a psychotherapeutic strategy, the

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Motivation-Focused Therapy, after another psychological treatment of individual CBT-E compared to individual CBT-E alone in ED outpatients.

Concerning the sequential addition of motivational-type therapies in mixed ED samples, no significant differences emerged between groups that underwent motivational interventions after or before the first level treatment and those that only underwent the first level treatment in terms of reduced ED symptomatology, reduced ED-related cognitive and psychological symptomatology or additional clinical variables like anxiety and depression symptoms, motivation or remission rates (Dean et al., 2008; Allen et al., 2012).

MacDonald et al. (2021) compared two maintenance psychological treatment modalities sequentially following intensive inpatient treatment, that is individual CBT versus intensive outpatient group treatment that also contained CBT. No significant differences were reported between groups in the considered outcomes which were a return to clinically significant symptoms as well as scores in weight and shape concerns. A return to symptoms was found at 12-month follow-up in a high percentage of patients (51.6%) independently of diagnostic category and maintenance treatment modality. While no comparison treatment group was available, the addition of a behavioural intervention called "sequential binge (SB)" sequentially following intensive CBT-E-based inpatient treatment was associated with further reductions in the planned food intake and number of binges (Neveu et al., 2016).

In terms of differences in drop-out rates in mixed ED, while the scope of motivational interventions is to reduce drop-out, the groups receiving motivational interventions exhibited similar treatment completion rates compared to the CBT groups (55.8% in Motivation Focused Therapy + CBT-E vs. 53.5% in CBT-E) (Allen et al., 2012) or compared to TAU (undefined) of an intensive inpatient treatment (percentages not reported) (Dean et al., 2008). Neveu et al. (2016) had a low rate of 13.3% drop-out at post-treatment of intensive treatment and SB ("sequential binge"), while no drop-out data was available in MacDonald et al. (2021).

4 | DISCUSSION

The present review aimed to explore the emerging literature on sequentially applied therapies and interventions in EDs and focused on providing an overview on the following aspects: identifying the sample characteristics of studies on sequential treatments in EDs, identifying the therapeutic approaches applied sequentially, study design characteristics, and effects of the sequential treatments in terms of reduced ED symptomatology, reduced ED-correlated symptomatology and on drop out.

In terms of sample characteristics, while age range was found to vary widely, most studies were limited primarily to BED patients, followed by mixed ED samples, or in the minority of cases, BN patients. Moreover, most studies contained exclusively female samples or females represented the majority of the sample with few male participants, likely representing the greater prevalence of EDs among women (Silén & Keski-Rahkonen, 2022). Not a single study on AN patients was identified. This is particularly surprising as sequential treatments are built to target standard-treatment resistant patients (Borbély et al., 2022) and AN patients are known for the difficulty in treatment engagement due to the greater egosyntonic nature of their illness (Gregertsen et al., 2017).

Interestingly, while the main rationales for applying a sequential approach are the lack of optimal response to first-line treatment, the presence of residual symptoms after treatment, and/or comorbidity (Fava, 1999), only a few of the selected studies targeted non-responders or treatment-resistant cases with the exception of Agras et al. (1995), Mitchell et al. (2002) and Neveu et al. (2016). Moreover, no study applied sequential interventions explicitly for comorbid psychiatric conditions or psychopathology in ED patients.

The presence of comorbid psychopathological aspects and treatment resistance may justify the application of a sequential treatment, however, to date no clinical guidelines exist regarding when or to whom a sequential approach should be applied, nor concerning combined/integrated treatments or single treatment in EDs. Only clinical judgement can thus guide clinicians in treatment choices when comorbid conditions are present or emerge. This could explain the reason of lack of studies using sequential treatment to explicitly target comorbidity in ED. Currently, a thorough diagnostic assessment with careful consideration of the longitudinal development of the ED is suggested (Dalle Grave et al., 2021; Tecuta et al., 2020; Tomba et al., 2019) to inform case conceptualisation to help determine whether comorbidity warrants a distinct treatment that precedes or follows treatment for the ED. Clinicians should determine whether the additional psychopathological aspects in EDs are attributable to the ED itself or a direct consequence of the ED, and therefore whether the comorbidity could improve with ED treatment or whether the comorbidity could interfere with it (Dalle Grave et al., 2021). Studies which apply the sequential approach to better examine its clinical utility in the treatment of comorbidity in EDs are missing and warranted to support the application on this approach for such purposes. Concerning treatment

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resistance, no shared clinical guidelines to date exist, despite it being a critical issue in EDs (Fassino & Abbate-Daga, 2013; Halmi, 2013; Treasure, 2019).

In terms of the type of treatment approaches present, with the exception of two studies that added a pharmacological treatment as sequential adjunct to other psychological treatments (Agras et al., 1994; Mitchell et al., 2002), most therapies tested sequentially were of a psychological nature or constituted a behavioural intervention as in the case of "sequential binge" (Neveu et al., 2016) and in the case of BWL and BWL programs (Agras et al., 1994, 1995, 1997; Grilo et al., 2011). The sequential approach using two psychological interventions is in line with the clinical guidelines which indeed recommend the use of various psychotherapeutic approaches in the treatment of ED psychopathology (APA, 2006, 2010; NICE, 2020), albeit not indicating a sequential application of such treatments. The intensive treatments including inpatient treatment or intensive outpatient hospital-based treatments such as day hospitals, were instead not described in great detail (Dean et al., 2008; MacDonald et al., 2021; Neveu et al., 2016). More specifically, there was missing information on whether the treatment was of a combined and integrated nature or if any therapeutic components (medical support, individual therapy, group therapy, nutritional support) were provided in a certain sequential order, and whether any therapeutic components were provided before implementing the sequential treatment that was object of the study. Such missing data further complicates interpretation of results in a sequential treatment perspective especially in mixed ED sample research studies.

In terms of specific psychological-theoretical paradigms and protocols, CBT and CBT-E were overwhelmingly present. However, the sequential treatment modalities which were added sequentially to CBT were heterogenous in nature as were types of therapies used in the comparison groups, making any conclusions drawn highly tentative. It is important to note that the treatment modalities were mostly psychological in addition to being treatments that are recommended by clinical guidelines, suitably applied to the appropriate ED diagnostic group for which the treatment is recommended (i.e. CBT-E for BN and BED, WL interventions for BED, motivational-type interventions for BN, IPT and self-help modules for BN and BED (APA, 2006, 2010; NICE, 2020)). Despite the outpatient level of care and group modalities prevailing, studies varied in settings. Please see Table 2 summarising study characteristics and relevant findings. Contrary to standard clinical guidelines (APA, 2006, 2010; NICE, 2020), one study (Mitchell et al., 2002) had a strictly pharmacological only treatment after a first phase of CBT, although the patients had been poor responders to the previous CBT treatment.

In terms of study design, all studies were longitudinal as established by the inclusion criteria, however as the explicit intent of the selected studies wasn't to test the superiority of the sequential model to standardized single treatments, most studies did not contain a single treatment group as a comparison condition with the exception of four studies (Agras et al., 1994; Allen et al., 2012; Grilo et al., 2011; Treasure et al., 1996), three of which included CBT or CBT-E as a single treatment comparison group (Allen et al., 2012; Grilo et al., 2011; Treasure et al., 1996) that showed no significant advantages of the sequential application of two or more sequential modalities of treatment compared to the single course of treatment. The remaining studies mostly compared two or more sequential treatments to each other (Agras et al., 1995; Dean et al., 2008; MacDonald et al., 2021; Mitchell et al., 2002; Treasure et al., 1999) or lacked a comparison group altogether (Agras et al., 1997; Neveu et al., 2016), thus limiting generalisability of the results especially concerning the advantage/disadvantage of single versus sequential treatment. Moreover, when longitudinal data for the compared treatment conditions were presented, they were presented mostly as total time effects, thus not following a dismantling design in which a specific effect of the addition of a second treatment can be discerned. No studies compared sequential treatments to combined/integrated treatments.

With respect to the effects of the treatments, interestingly, several studies were characterised by the lack of differences in primary outcomes between treatment groups that received IPT (Agras et al., 1994, 1995; Mitchell et al., 2002), motivational type interventions (Allen et al., 2012; Dean et al., 2008) and BWL-based programs (Agras et al., 1994) and those that did not. The absence of significant differences in improvements in ED symptomatology or ED-correlated symptomatology between treatment conditions might be due to methodological issues including small treatment subgroup samples. Moreover, the samples of the selected studies might not have been appropriate for the treatments offered as sequential treatments should be reserved for patients with residual symptoms from previous treatments, treatment-resistant patients or patients with previous treatment failures as well as patients with comorbidities (Fava, 1999). The same considerations could be extended to the lack of significant differences within studies comparing different sequential treatments or a sequential treatment to a single treatment in drop-out rates, a finding that was reported in several studies (Agras et al., 1994; Allen et al., 2012; Dean et al., 2008; Mitchell et al., 2002; Treasure et al., 1996, 1999).

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Additionally, the lack of significant findings might be ascribable to the narrow clinical outcomes which were reported. For example, in studies on BED patients, studies maintained a strict focus on diagnosis-specific criteria, such as WL and binge-eating behaviours, while studies on BN patients focused primarily on reporting reduced binging-purging, use of laxatives or abstinence from binging and purging. More specifically, one study on BN patients did include measures which encompassed a more comprehensive range of symptoms assessed through the ED Examination instrument (Fairburn & Cooper, 1993) as well as through the Bulimic Thoughts Questionnaire (Franko et al., 1986) and the Three Factor Eating Questionnaire (Stunkard & Messick, 1985), however comparisons between treatment groups in such scores were not reported (Mitchell et al., 2002). The remaining studies on participants with BN (Treasure et al., 1996, 1999) didn't include additional psychological aspects beyond BN-specific behaviours and diagnostic criteria. The same cannot be said of the mixed ED group studies (Allen et al., 2012; Dean et al., 2008; MacDonald et al., 2021) which did include and report ED-related symptomatology encompassing cognitive and psychological aspects of ED captured by gold standard ED assessment tools including the ED Inventory (EDI-2, Garner, 1991) and Eating Disorder Examination-Q (EDE-Q, Fairburn & Beglin, 1994). Indeed, such studies did find significant differences between treatment groups that were previously discussed.

A more comprehensive and broad definition of ED psychopathology treatment outcome encompassing additional ED-specific or ED-related psychological elements such as the identified ED maintenance factors (Fairburn et al., 2003) of clinical perfectionism, interpersonal problems and low self-esteem or the more recently non-core symptomatology identified through network analyses as salient in EDs such as ineffectiveness, interoceptive awareness, and affective problems (Monteleone & Cascino, 2021) might have revealed important differences in treatment comparisons. Additional facets of EDs identified by ED researchers which are not necessarily diagnostic, such as body-checking and body anxiety, food addiction behaviours, and food-related anxiety, in addition to ED-related mood disturbance and other areas of compromised functioning regarding one's social life, quality of life and psychological well-being (Tomba et al., 2014, 2017) might have also yielded differing results. Such neglected domains denote important clinical markers of treatment response and remission (Tomba et al., 2019).

An additional fundamental aspect to appraise when formulating and testing sequential treatments is not only broadening the clinical outcome one considers, but also carefully selecting the appropriate measures that correspond to the targeted areas of an intervention. Thus, it would be more appropriate to expect improvements in the newly targeted areas of the secondary treatment approach (e.g. psychological) rather than expect further improvements in the symptoms targeted by the preceding treatment (e.g. behavioural weight loss). For example, one should expect psychotherapy with an interpersonal component to improve interpersonal difficulties rather than necessarily expecting it to further reduce binge-eating which is the target of CBT-based protocols, such as in the USH manual, as was expectedly found in one study (Tasca et al., 2018). Indeed, one of the rationales for using a sequential approach is that treatments offered in sequential order should yield, in order to reach a more pervasive level of recovery, a unique and separate contribution to a patient's well-being (Fava, 1999).

Other issues that were raised in the selected studies in explaining the lack of differences between treatment modalities pertained to sequential treatments being perhaps too long and therefore unacceptable for patients (Mitchell et al., 2002), treatments being characterised by different time frames and intensities which may be equally beneficial thus not yielding different results (MacDonald et al., 2021), or elements of additional modules being counterproductive as in the case of motivational therapy. For example, as suggested in Dean et al. (2008)'s study, motivational interventions might in reality impede progress by normalising and encouraging the patient to remain in the contemplation process, at the expense of progressing to the following phase of motivation, that is, behavioural and attitudinal change. In another study a further possible detrimental effect of sequential treatment emerged that clinicians should carefully consider. In particular, Agras et al. (1995) reported an increase in binge eating and weight after patients had concluded IPT as a sequential treatment to CBT although these changes were not statistically significant. Such worsening effects could, however, underscore the non-responsiveness of patients, since those that had been assigned to IPT had not obtained optimal results with the preceding treatment of standard CBT. While iatrogenic factors of treatments are widely studied in the medical field, to date, such detrimental and effects in psychological treatments in EDs are understudied as there is also a lack of shared criteria in the literature to identify them (Gardini et al., 2022) and should be an additional factor to consider in sequential approaches.

While the here presented literature does not seem to offer yet clear answers regarding the advantages or disadvantages of sequential treatments in EDs, one clinically useful aspect of the reviewed studies is uncovering potential alternative treatments that may be as effective as

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first-line therapies and may be helpful when first line treatments are unavailable. One such study was provided by Grilo et al. (2011) where three treatment conditions, CBT alone, BWL alone, and CBT + BWL, did not differ significantly in their effects on any time points on remission from binge-eating, motivating authors to consider that offering BWL as an alternative to CBT when CBT is unavailable to BED patients might be a useful strategy. Additionally, a few studies (MacDonald et al., 2021; Treasure et al., 1996, 1999) support the notion that the less intensive or cost-effective secondary therapy obtained results that did not differ significantly from those obtained by the more intensive therapeutic alternative in terms of number of sessions (Treasure et al., 1996), in terms of format (Treasure et al., 1999) or in terms of level of care (MacDonald et al., 2021), indicating that a sequential treatment comprised of a cost-effective intervention preceded or followed by standard treatment might obtain possibly similar results compared to only providing the standard or intensive full treatment.

5 | CONCLUSIONS

Overall, several important gaps in the literature on sequential treatments in EDs can be identified. First and foremost, only a few studies examined the advantages of a sequential treatment that comprised a primary treatment plus a secondary treatment for residual symptomatology compared to applying a single treatment. Moreover, the lack of such data in the literature might only be apparent and have been due to limitations posed by the systematic review process of our scoping review which limits the search to studies found with specific keywords, implying the exclusion of other possibly relevant data. Indeed, ED standard treatment trials might constitute sequential treatments where two modalities of interventions are applied in a temporally sequential manner to improve outcomes and residual symptoms, but they are at the moment not identified as such. The term sequential is rarely used in the literature in reference to such treatments, especially those concerning treatment resistance cases (Wonderlich et al., 2012) representing an obstacle to detect research on the sequential approach in EDs.

Additionally, in the studies that are available, this scoping review underscores the lack of studies on AN patients and male patients, studies with an appropriate control treatment group as comparison to the sequential treatment object of study, as well as studies which consider a wider range of psychological outcomes not limited to BMI and traditionally considered core eating psychopathology.

Given the promising results of the sequential model obtained in other hard-to-treat clinical populations at high risk of relapse such as depression (Guidi et al., 2011, 2016; Guidi & Fava, 2021), future studies should elucidate whether EDs could benefit from such treatments. Future studies should test sequential models in AN patients, include male participants, participants that have previous treatment failures, are poor responders to standard treatments and/or have comorbidities and residual ED symptomatology after treatment. Moreover, future studies would benefit from the inclusion of appropriate control comparison groups (i.e., a single standard recommended treatment) in order to better discern the possible additive effects of the sequential model in EDs. Eating disorder treatment may also benefit from randomized controlled trials that specifically compare sequential approaches to already considered golden standards of ED treatment to improve maintenance of treatment gains, in addition to reducing the probability of relapse (Tomba et al., 2019).

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CONFLICT OF INTEREST STATEMENT

The authors report that there are no competing interests to declare.

DATA AVAILABILITY STATEMENT

Due to the non-empirical nature of the work (systematic review) no original data was collected for this article.

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