Pharmacological Research 216 (2025) 107782

Contents lists available at ScienceDirect

Pharmacological Research

journal homepage: www.elsevier.com/locate/yphrs

The pharmacological treatment of anxiety in people with eating disorders: A systematic review

Rebecca Morris [a,*], Johanna Keeler [a], Janet Treasure [a,b], Hubertus Himmerich [a,b]

[a] Department of Psychological Medicine, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
[b] Eating disorder unit, Bethlem Royal Hospital, South London and Maudsley NHS Foundation Trust (SLaM), London, UK

ARTICLE INFO

Keywords:
Anorexia nervosa
Bulimia nervosa
Binge eating disorder
Avoidant restrictive food intake disorder
Eating disorders
Anxiety
Pharmacological treatment

ABSTRACT

People with eating disorders experience high rates of psychiatric comorbidities, including anxiety disorders such as generalised anxiety disorder, social anxiety disorder and specific phobias. Anxiety can influence the prognosis of an eating disorder, by worsening symptoms, and acting as a barrier to treatment. Therefore, targeting treatment efforts towards anxiety may improve eating disorder outcomes. The primary aim of this systematic review was to summarise the evidence base for the pharmacological treatment of anxiety symptoms in people with eating disorders. An electronic search of three databases (PubMed, Medline, and PsycInfo) was conducted. Papers were included if they investigated pharmacotherapy (antidepressants, antipsychotics, antianxiety, psychedelics, etc.) in eating disorder samples, with primary or secondary outcomes of anxiety. A total of 51 studies were included, and results were mixed across drug classes documenting both favourable and non-significant anxiety outcomes. There was evidence for the use of fluoxetine for anxiety in anorexia and bulimia nervosa, but not for binge eating disorder. Evidence for the use of olanzapine was documented for anxiety in AN, and preliminary case reports suggested its use in ARFID for anxiety symptoms. Preliminary evidence for developing pharmacological agents, such as psilocybin and ketamine, reported favourable outcomes in AN patients. More RCTs are required to explore efficacy and safety of pharmacological agents in treating anxiety in people with eating disorders.

1. Introduction

1.1. Eating disorders

Eating disorders (EDs) are complex psychiatric disorders characterised by disturbances in eating and weight behaviours, with severe physical and psychological consequences [109,122]. EDs have a multifactorial nature, with involvement of biological, social, and psychological processes [109]. The International Classification of Diseases 11th Revision (ICD-11) recognises the following eating disorders: Anorexia Nervosa (AN), characterised by restrictive eating that causes significantly low weight, Bulimia Nervosa (BN), characterised by episodes of binge eating followed by compensatory behaviours, Binge Eating Disorder (BED), characterised by binge eating without compensatory behaviours, Pica, Rumination disorder, Avoidant Restrictive Food Intake Disorder (ARFID), as well as unspecified and other specified feeding and eating disorders (UFED; OSFED) [124].

People with EDs often present with psychiatric comorbidities, particularly affective and anxiety disorders, which act as poor prognosis markers, and can significantly alter the course of disorder and increase the mortality rate [56], as well as act as barriers to treatment [38].

1.2. Comorbid anxiety in eating disorders

1.2.1. Anxiety disorders

Anxiety disorders are highly prevalent psychiatric disorders that are associated with extensive impairment [10]. Recognised anxiety disorders in the DSM-5 include generalised anxiety disorder (GAD), social anxiety disorder (SAD), panic disorder (PD), specific phobia, agoraphobia, selective mutism, and separation anxiety [2]. Characteristics and recommended treatment options can be seen in Table 1.

1.2.2. Anxiety in people with EDs

People with EDs often experience anxiety as a psychiatric comorbidity, with 65 % of women undergoing ED treatment meeting criteria for at least one anxiety disorder [105]. It is important to distinguish

* Corresponding author.
E-mail address: rebecca.c.morris@kcl.ac.uk (R. Morris).

https://doi.org/10.1016/j.phrs.2025.107782
Received 30 January 2025; Received in revised form 13 April 2025; Accepted 13 May 2025
Available online 14 May 2025

between anxiety disorders as comorbidities and eating-related anxiety experienced in EDs. Anxiety-eliciting eating situations may include eating new food, in novel restaurants, and eating in front of other people, such as friends, family, and people who are perceived to be thinner or who are eating less [121]. Anxiety disorders often comorbid with EDs include generalised anxiety disorder (GAD), specific phobias, and social anxiety disorder (SAD) [82]. In patients with diagnosed EDs, rates of anxiety comorbidity are between 45.4 % and 55 % [118].

1.2.2.1. Anxiety predisposing to EDs. Individuals typically report that the onset of their anxiety disorder preceded the onset of their ED [57, 105], with anxiety disorders predating ED onset in 75 % of AN and 88 % of BN patients [37]. Longitudinal analyses support this chronology of appearance, with initial diagnoses of OCD increasing the risk of later diagnoses of AN [22], and latent factors that reflected GAD symptoms were related to increased ED cognitions and behaviours four years later [97]. This study also reported that physical anxiety predicted the onset of BN, and that worry predicted the onset of AN and disordered eating [97]. This suggests that the presence of an anxiety disorder may predispose individuals to the development of an ED.

Genetic links between anxiety and EDs note that the presence of one disorder significantly increases the likelihood of another, with heritability estimates between 40 % and 60 % [108,118,122]. Genetic correlations have been found between AN and OCD [22,125], although OCD is no longer classified as an anxiety disorder in the DSM-5.

1.2.2.2. Rates of anxiety disorders in EDs. Rates of anxiety disorders in EDs vary between disorder, with rates of SAD being found in 84.5 % of BN patients, and 75 % of BED and AN-binge purge (AN-BP) patients [60]. Additionally, GAD was found to be higher in AN-BP (35 %) and BN (31.9 %) than BED (25.9 %) and AN-Restrictive (AN-R; 27.9 %) [118]. Similarly, rates of obsessive-compulsive disorder (OCD) were higher in AN than BN [66,118], and some studies show higher rates of OCD in AN-BP than AN-R, although others have not consistently supported this finding [1].

1.2.3. Anxiety as prognostic markers in EDs

Psychiatric comorbidity in EDs complicate the treatment and recovery process by exacerbating ED symptomatology [122]. High levels of anxiety are related to greater ED chronicity, being linked with severity of ED psychopathology, hospitalisation frequency, treatment compliance, and illness duration [82,91]. Lower levels of treatment

Table 1
Anxiety disorders according to DSM-5 and recommended pharmacological and psychotherapy according to the World Federation of Societies of Biological Psychiatry guidelines for the treatment of anxiety.

Disorder[a]	Characteristics[a]	Recommended Psychotherapy[b]	Recommended Pharmacotherapy[b]	Recommended combination[b]
Generalised Anxiety Disorder (GAD)	Excessive worry which is difficult to control and encompasses a variety of concerns. The worry is associated with other symptoms, including fatigue and sleep disturbance. The worry or physical symptoms cause significant distress or impairment.	CBT	SSRIs (escitalopram, paroxetine, sertraline) SNRIs (venlafaxine, duloxetine) Agomelatine TCA (imipramine) Pregabalin Vilazodone Benzodiazepines (alprazolam, bromazepam, diazepam, lorazepam) In adolescents, SSRI fluvoxamine, fluoxetine, and sertraline. SNRIs duloxetine and venlafaxine	In adolescents, combined sertraline and CBT
Panic Disorder (PD)	Recurring panic attacks that may include symptoms of sweating, nausea, light-headedness, and/or shaking. May be followed by persistent worry about panic attacks, and/or avoidance behaviours.	CBT iCBT	SSRIs (citalopram, escitalopram, fluvoxamine, fluoxetine, paroxetine, sertraline) SNRI venlafaxine TCAs (imipramine, clomipramine) Benzodiazepines (alprazolam, clonazepam, diazepam, lorazepam)	CBT + drug
Selective Mutism	Does not speak in specific social settings, such as school, despite adequate language competence displayed in other settings, like home.	No strong evidence for recommendation	No strong evidence for recommendation	No strong evidence for recommendation
Separation Anxiety Disorder	Inappropriate or excessive anxiety concerning separation from those to whom they are attached.	No strong evidence for recommendation	SSRIs (fluvoxamine, escitalopram, fluoxetine) SNRIs (duloxetine, venlafaxine)	Sertraline and CBT
Social anxiety disorder (SAD)	Worry about social situations, including interactions, observations, and/or performances, due to fear of being negatively evaluated. These situations provoke fear or anxiety that is disproportionate to the actual threat posed and are often avoided.	CBT (adult and adolescent) iCBT	SSRIs (escitalopram, fluvoxamine, paroxetine, sertraline, citalopram) SNRI venlafaxine Pregabalin Phenelzine Moclobemide Mirtazapine Gabapentin Benzodiazepines (bromazepam, clonazepam) In adolescents, SSRI paroxetine and SNRI venlafaxine	No strong evidence for recommendation
Specific Phobia	Worry about a specific object or situation, such as flying, injections, or blood. These phobias provoke fear or anxiety that is disproportionate to the actual threat posed and are often avoided.	Exposure Virtual reality exposure CBT	Benzodiazepine midazolam Midazolam Alprazolam Pregabalin Paroxetine	No strong evidence for recommendation

Notes. [a]Information on disorders and characteristics as in [2]; [b]Based on treatments with a recommendation grade of 1 or 2 in [5]. Abbreviations: CBT = cognitive behavioural therapy; iCBT = internet interventions based on cognitive behavioural therapy; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin and norepinephrine reuptake inhibitor.

engagement and help-seeking have been associated with higher levels of SAD [38]. These findings necessitate the importance of targeting anxiety in ED treatment and management as a means of improving ED outcomes [95,122].

1.3. Defining recovery and remission in ED research

Considering the prognostic value of anxiety and the bidirectional relationship between EDs and anxiety disorders, anxiety may be important as a transdiagnostic outcome across ED research and precision treatment targeting anxiety symptoms and comorbidities may improve ED outcomes. This may be of particular interest in AN, where recovery and remission is often conceptualised and measured by weight restoration, which although central to recovery, is not sufficient as a single outcome [9]. People with EDs have expressed that whilst weight restoration is important, focus on this has led to underappreciation of psychological components of their ED [9]. Given that psychological symptoms, such as anxiety, are maintenance factors in AN, that worsen symptomatology [122] and drive treatment dropout and relapse, a weight-based end goal should not be expected to equal psychological symptom remission [77].

1.4. Current treatments for anxiety in eating disorders

1.4.1. Psychological treatment

NICE guidelines recommend psychological therapies as a first line of treatment for eating disorders [78]. The Maudsley Model of Treatment of Anorexia Nervosa for Adults (MANTRA) is recommended by NICE for AN; MANTRA is based on the cognitive interpersonal maintenance model of AN and addresses the emotional and cognitive maintenance factors of AN through adaptive coping methods [98]. Whilst not specifically developed for anxiety in AN, improvements in anxiety were found after MANTRA in an RCT [18].

Exposure-based approaches for AN have reported that pre-meal anxiety, anxiety after eating, and general anxiety were significantly reduced following exposure therapy [70,71]. Furtherly, augmenting d-cycloserine to exposure therapy resulted in a significantly lower post-meal anxiety score than exposure with placebo [104].

1.4.2. Pharmacological treatment

Currently, pharmacological treatment options that are approved in some countries include fluoxetine for BN and lisdexamfetamine for BED [50], but there is no medication approved for the treatment of AN [48]. For an in-depth review of pharmacological treatment in EDs, see the recent update of the World Federation of Societies of Biological Psychiatry (WFSBP) recommendations [49].

1.5. Aims of this review

Despite the high levels of comorbidity between eating and anxiety disorders, the treatment of anxiety symptoms in these individuals remains a clinical challenge. Addressing these wider aspects of psychiatric distress and helping individuals learn to manage these symptoms may improve outcomes in the long-term, which is often highlighted as a priority by individuals with lived experience. One missing piece is the lack of clear guidelines for the pharmacological treatment of anxiety symptoms in people with EDs. This systematic review aims to:

(a) Summarise the evidence base for pharmacological agents in treating anxiety symptoms in populations of people with eating disorders
(b) Rate the level of evidence for pharmacological agents in treating anxiety symptoms in populations of people with eating disorders
(c) Discuss future research for the treatment of anxiety symptoms in populations of people with eating disorders

2. Methodology

This systematic review follows the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; [81]).

2.1. Study identification

A systematic search of electronic databases PubMed, Medline, and PsycInfo was performed. The final search was conducted on 12th March 2025. Additional manual searching on Google Scholar and through reference lists of eligible publications was also conducted. Search terms were derived from the WFSBP anxiety guidelines [5]; drug classes that were given a grade of recommendation of one or two were included in the search terms. The following search terms were used (binge eating OR bulimi* OR anorex* OR avoidant-restrictive OR eating OR eating disorder) AND (anxi* OR anxiety OR panic) AND (antidepress* OR anxiolytic OR antipsychotic OR psychedelic OR anticonvulsant); see supplementary materials (Table S1) for the full search strategy. The limiters English language, peer-review, and human population were applied where possible. See Fig. 1 for the PRISMA flowchart.

2.2. Eligibility criteria

Identified studies were reviewed to evaluate whether they met the following inclusion criteria: (1) participants had anorexia nervosa, bulimia nervosa, binge eating disorder, avoidant-restrictive intake disorder, eating disorder not otherwise specified, other specified feeding and eating disorder, or unspecified feeding or eating disorder, or any other eating disorder; (2) studies investigated a pharmacological treatment (antidepressants, antipsychotics, anxiolytics, stimulants, anticonvulsants, and psychedelics); (3) studies recorded and reported anxiety symptoms. There were no restrictions on the age of participants, nor the duration or onset age of their ED, nor how diagnosis was determined. There were also no restrictions to the data type (quantitative or qualitative) or type of anxiety measure.

Exclusion criteria was as follows: (1) systematic reviews, meta-analyses, commentaries, reviews, or conference abstracts; (2) studies that investigated psychological, hormonal or dietary interventions; (3) studies that used animal subjects; (4) studies that were not written in the English language.

Studies are presented firstly by drug class, then eating disorder diagnosis, and finally by quality ranking.

2.3. Study selection

One reviewer (RM) screened titles and abstracts using EndNote 21 [107]. Two reviewers (RM and JLK) then independently screened the full texts of the resulting articles against the inclusion criteria to determine their eligibility. The reviewers met to discuss and resolve any discrepancies.

2.4. Data extraction

The primary reviewer (RM) extracted study design, country, ED diagnosis, anxiety comorbidity, BMI, intervention and comparator (including agent type, dose, and duration), anxiety measure tool, and the follow-up anxiety outcomes. Any missing information was noted as not reported.

2.5. Quality assessment

Studies that met the inclusion criteria were quality assessed using the Joanna Briggs Institute critical appraisal tools [74,75,116]. The quality assessments were initially undertaken independently by one reviewer (RM) and 50 % were verified by an experienced second reviewer (JLK).

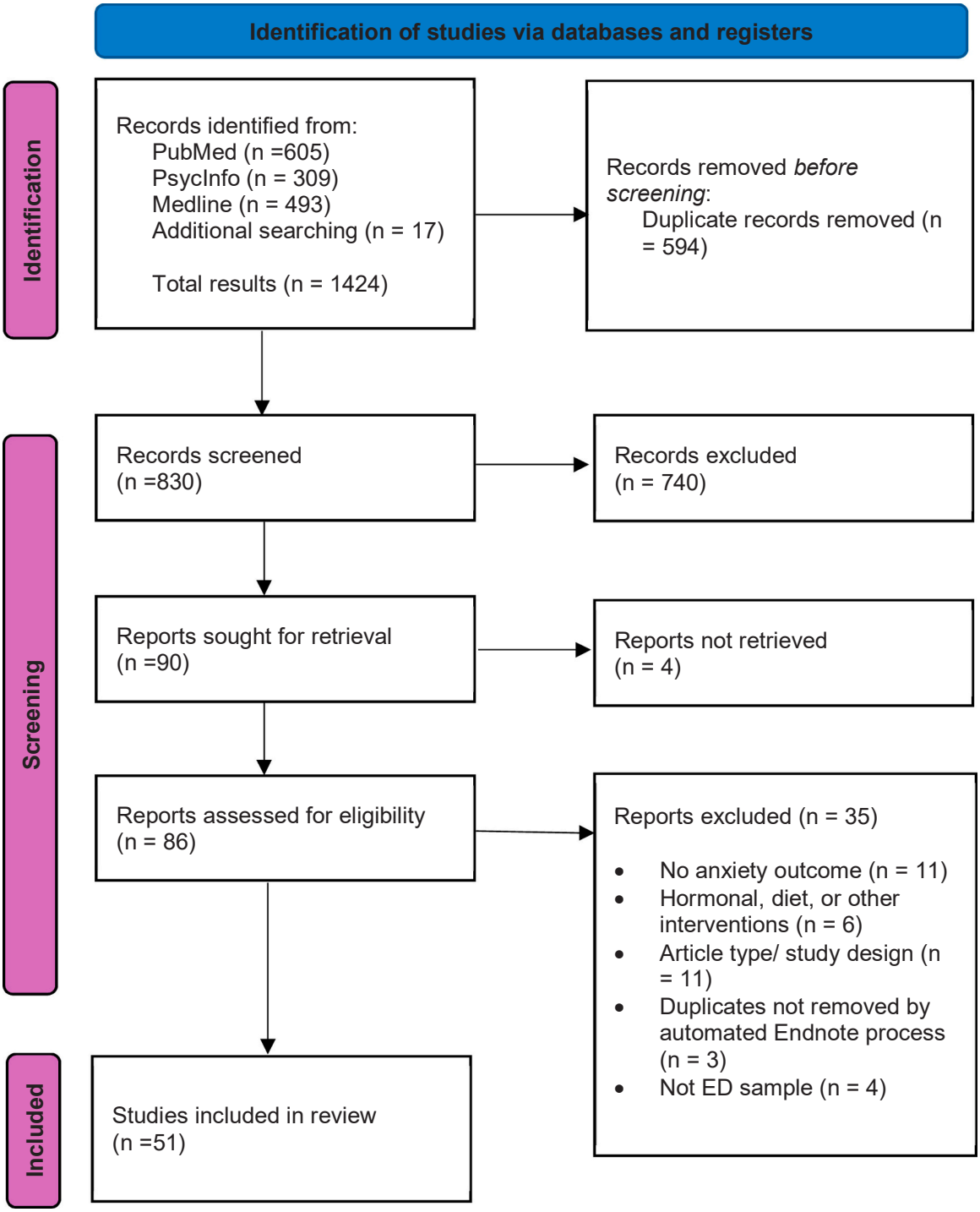

Fig. 1. PRISMA Flowchart.

All studies were included regardless of quality.

3. Results

3.1. Results of search

The search flow chart is reported in Fig. 1. Out of 1424 articles found in the search; after removal of duplicates 830 remained and were screened. Following this 86 full texts were retrieved and screened, leaving 51 studies included in the systematic review.

Of the 51 included articles, there were 16 RCTs, 16 open-label studies, 10 case reports, four case series, and five retrospective studies (including chart reviews and cohort studies).

Among those included, 25 assessed antidepressants, 15 assessed antipsychotics, two assessed anxiolytics, three assessed anticonvulsants, one assessed stimulants, and five assessed psychedelics and cannabinoids.

A variety of anxiety measures were included: Hamilton Anxiety Rating Scale (n = 12), Symptom Checklist-90 (n = 2), Symptom Checklist-58 (n = 1), Beck Anxiety Inventory (n = 2), State Trait Anxiety Inventory (n = 9), Hamilton Anxiety Rating Scale (n = 2), Hopkins Symptom Checklist (n = 1), Self-report for Childhood Anxiety Related

Disorders (n = 1), State Trait Anxiety Inventory-X (n = 1), Mood and Anxiety Symptom Questionnaire (n = 1), Multidimensional Anxiety Scale for Children (n = 2), Spielberger State-Trait Anxiety Inventory-State (n = 1), Spielberger State-Trait Anxiety Inventory- Trait (n = 1), Physical Appearance State and Trait Anxiety (n = 1), Generalised Anxiety Disorder Scale-7 (n = 1). 13 studies did not report the measure used, and one study devised their own questionnaire.

Regarding sample characteristics, the BMI of participants varied greatly across all studies, ranging from 11.8 to 45.0 kg/m^2. The mean age of participants across studies ranged 8–45 years old; of those studies that reported an age range, 22 included participants under the age of 18. 22 of the included studies reported the presence of comorbid anxiety disorders in their sample: GAD (n = 6), with 38–100 % of participants reporting this comorbidity across the samples; panic disorder, (n = 3) with 2–33 % of participants reporting panic disorder across the samples; anxiety disorder, including anxiety not otherwise specified and anxiety disorder unspecified, (n = 12) with 12–100 % of participants across the samples reporting this comorbidity; social phobia (n = 2), with 12–47 % of participants reporting this comorbidity across samples; specific phobia (n = 2), with 53–100 % of participants reporting this across samples; OCD (n = 12), with 2–100 % of participants across samples reporting comorbid OCD; and separation anxiety disorder (n = 1), with 100 % of the sample reporting this comorbidity.

There were 26 studies for AN [3,4,6,12,14,15,24,26,30,44,58,64,68,79,85,87,88,90,92,96,99,101,103,115,120,123], 13 for BN [7,13,17,23,31,32,33,54,61,72,94,100,119], six for BED [19,20,39,42,43,89], five for ARFID [16,41,80,102,106], and one for PTFD [11].

3.2. Quality assessment of included studies

The quality of included studies is reported in Tables S2–6. All studies were included in the review following appraisal using JBI critical appraisal tools [74,75,116].

All case reports scored over 60 %, with three scoring 100 % [12,80,123]. Two case series scored 80 % [92,99], one scored 50 % [102] and one scored 30 % [7].

Eight studies appraised with the RCT tool scored over 75 % [3,33,39,43,44,54,58,120]. Ten studies scored between 50 % and 75 % [103,119,24,30,31,72,88–90,94]. The remaining three studies scored slightly below 50 % [13–15].

Two studies appraised with the quasi-experimental tool scored 100 % [96,101]. Eight studies scored above 50 % [4,6,20,42,61,79,85,87]. The remaining one study scored just below 50 % [100].

Finally, two studies evaluated with the cohort tool scored over 50 % [19,68]. The remaining three studies scored under 50 % [16,41,64].

3.3. Antidepressants

Characteristics of included studies can be seen in Table 2.

3.3.1. Fluoxetine (SSRI)

3.3.1.1. Fluoxetine studies in anorexia nervosa. An RCT of fluoxetine (m = 38 mg/day, sd= 21 mg/day) versus placebo documented no significant effect of drug or time on anxiety, but reported that AN-R patients who remained on fluoxetine for one year had significant reductions in anxious mood as measured by HARS from baseline to one year [58]. A double-blind placebo-controlled randomised trial comparing 60–80 mg/day of fluoxetine (n = 49) and placebo (n = 44) for one year in AN patients reported significantly higher reductions in anxiety symptoms measured by the BAI in the fluoxetine group [120].

An open label study of 60 mg/day of fluoxetine (n = 15) versus 75 mg/day of nortriptyline (n = 7) for four months in 22 AN-R patients reported significant progressive decreases in anxiety as measured by the HAM-A in both treatments, with nortriptyline significantly more effective than fluoxetine in reducing anxiety [14]. When comparing 60 mg/day of fluoxetine (n = 6) and 300 mg/day of amineptine (n = 7) for four months, a significant improvement in anxiety measured by HAM-A was reported in 13 AN-BP patients, but no significant difference between groups was evidenced [15]. A preliminary controlled trial of 40 mg/day of fluoxetine (n = 12) and 75 mg/day of venlafaxine (n = 12) for six months in 24 atypical AN patients, two with comorbid OCD, documented significant reductions in anxiety on the STAI only in the venlafaxine group [90].

3.3.1.2. Fluoxetine studies in bulimia nervosa. Fluoxetine is approved by the U.S. Food and Drink Administration (FDA) for the treatment of BN and is proven to be safe and effective in this population [61,76].

Older research suggests that 60 mg/day of fluoxetine (n = 22) for 8 weeks significantly decreased anxiety symptoms compared to placebo (n = 24), both in clinical and self-rated anxiety measures, in a double-blind placebo-controlled RCT of 46 BN patients [54]. An open clinical trial of 60 mg/day of fluoxetine (n = 10) in BN patients over eight weeks documented a significant reduction in anxiety based on SCARED (self-reported for childhood anxiety related disorders) [61]. In an open label uncontrolled study of 10 BN patients on 80mg/day for three months, patients had reduced trait anxiety on the STAI [100].

3.3.1.3. Fluoxetine studies in binge eating disorder. An RCT of 60 mg/day of fluoxetine versus 300 mg/day fluvoxamine in 108 BED patients reported significant reduction in anxiety in the fluvoxamine group, but not in the fluoxetine group, after 24 weeks of treatment [89]. One year after treatment ended, STAI-1 scores had significantly increased in fluoxetine group [89].

3.3.2. Sertraline (SSRI)

3.3.2.1. Sertraline studies in anorexia nervosa. An open controlled trial of 50–100 mg/day of sertraline for 14 weeks in the treatment of 11 AN-R patients reported a decrease in anxiety on the SCL-58 with a trend towards significance at $p < .001$ [96].

3.3.3. Citalopram (SSRI)

3.3.3.1. Citalopram studies in anorexia nervosa. In 39 AN-R patients randomised to 10–20 mg/day of citalopram (n = 19) or wait list (n = 20) for 12 weeks, citalopram had a significant reduction in anxiety on the SCL-90 [30].

3.3.4. Fluvoxamine (SSRI)

3.3.4.1. Fluvoxamine studies in bulimia nervosa. A double-blind placebo-controlled comparison of fluvoxamine (n = 37) and placebo (n = 35) over 15 weeks documented no superiority of fluvoxamine versus placebo in reducing anxiety on the HSCL [33].

An early open label trial of 300 mg/day fluvoxamine (n = 10) versus 300 mg/day amineptine (n = 5) over four months reported that anxiety on the HRS-A did not significantly change in the fluvoxamine group, but did significantly reduce in the amineptine group [13].

3.3.5. Duloxetine (SNRI)

3.3.5.1. Duloxetine studies in bulimia nervosa. A case study of one BN patient with comorbid GAD was given 30 mg/day of duloxetine, increasing to 60 mg/day, over a 12-week period; the patient reported marked reductions in GAD symptoms [23].

3.3.5.2. Duloxetine studies in binge eating disorder. A placebo-controlled RCT of 40 BED patients, randomised to either duloxetine (m = 78.7 mg/day) or placebo showed no significant difference between groups in

Table 2
Characteristics of included studies testing antidepressant medication.

	Study Reference	Country	Study Design	ED (N)	Comorbid Anxiety (N)	Drug Agent (N)	Dose mg/day (m/sd)	BMI m(sd)	Comparator Comparator (N)	Dose mg/day (m/sd)	BMI m(sd)	Treatment Length	Follow-Up	Anxiety Measure	Results
Anorexia Nervosa															
	Brambilla et al. [14]	Italy	Open label	AN-R (22)	NR	Fluoxetine (15)	60	14.7 (1.5)	Nortriptyline (7)	75	15.9 (1.9)	4 months	1, 2, and 4 months	HAM-A	Significant decrease in anxiety in both treatment. Nortriptyline significantly more effective than fluoxetine
	Brambilla et al. [15]	Italy	Open label	AN-BP (13)	NR	Fluoxetine (6)	60	16.7 (2.2)	Amineptine (7)	300	16.3 (2.8)	4 months	1, 2, and 4 months	HAM-A	Significant decrease in anxiety, but no difference between groups
	Fassino [30]	Italy	RCT	AN-R (39)	NR	Citalopram (19)	10 increased to 20	16.19 (0.81)	Waitlist (20)	NA	15.62 (1.42)	12 weeks	12 weeks	SCL−90	Citalopram significantly greater reduction in anxiety than wait list
	Kaye et al. [58]	USA	RCT	AN-R (35)	NR	Fluoxetine (16)	38 (21)	NR	Placebo (19)	20	NR	4 weeks to 1 year	4 week intervals up to 1 year	HARS	Patients on fluoxetine for 1 year had reductions in anxiety. No difference between groups.
	Noma [79]	Japan	Open label	AN-BP (6) BNp (7) BNnp (7)	NR	Milnacipran (20)	37 (14.1) titrated to 60 (22)	14.7 (1.3) 20.0 (1.8) 23.5 (6.2)	NA	NA	NA	8 weeks	8 weeks	HAM-A	Significant anxiety improvement at 8 weeks
	Ricca et al. [90]	Italy	Controlled trial	Atypical AN (24)	OCD (2)	Fluoxetine (12)	40	15.84 (0.46)	Venlafaxine (12)	75	15.67 (0.59)	6 months	6 months	STAI	Only venlafaxine significantly reduced anxiety
	Santonastaso et al. [96]	Italy	Open controlled trial	AN-R (22)	NR	Sertraline (11)	50 raised to 100 in 4 patients after 1 months	15.8 (1.1)	No medication (11)	NA	16.4 (0.9)	14 weeks	14 weeks	SCL−58	Non-significant decrease in anxiety
	Walsh et al. [120]	USA	RCT	AN (93)	NR	Fluoxetine (49)	60–80	20.16 (0.48)	Placebo (44)	60–80	20.45 (0.51)	1 year	1 year	BAI	Significantly greater anxiety reduction in fluoxetine than placebo
Bulimia Nervosa															
	Brambilla et al. [13]	Italy	Open label	BN (15)	NR	Fluvoxamine (10)	300	NR	Amineptine (5)	300	NR	4 months	4 months	HRS-A	Significant anxiety reduction in amineptine. No

(*continued on next page*)

Table 2 (*continued*)

	Study Reference	Country	Study Design	ED (N)	Comorbid Anxiety (N)	Drug Agent (N)	Dose mg/day (m/sd)	BMI m(sd)	Comparator Comparator (N)	Dose mg/day (m/sd)	BMI m(sd)	Treatment Length	Follow-Up	Anxiety Measure	Results
															significant reduction in fluvoxamine.
	Christensen and Averbuch [23]	USA	Case Study	BN (1)	GAD	Duloxetine	30 increased to 60	NR	NA	NA	NA	12 weeks	12 weeks	NR	Marked reduction in GAD symptoms
	Fassino et al. [31]	Italy	Randomised open label	BN (28)	Excluded if axis 1 disorder	Reboxetine	2–4	21.26 (4.09)	NA	NA	NA	12 weeks	12 weeks	HAM-A	No significant anxiety reduction
	Fichter et al. [33]	Germany	Double blind placebo controlled comparison	BN (72)	NR	Fluvoxamine (37)	50–150	NR	Placebo (35)	4.4 capsules	NR	15 weeks	16 weeks	HSCL	No superiority of fluvoxamine versus placebo for anxiety
	Kanerva, Rissanen, and Sarna [54]	Finland	RCT	BN (46)	OCD (2)	Fluoxetine (22)	60	NR	Placebo (24)	60	NR	8 weeks	8 weeks	NR	Significant decrease in anxiety compared to placebo
	Kotler et al. [61]		Open clinical trial	BN or EDNOS (10)	NR	Fluoxetine (10)	60	22.3 (2.5)	NA	NA	NA	8 weeks	8 weeks	SCARED	Significant anxiety reduction
	Mitchell [72]	USA	RCT	BN (155)*	NR	Imipramine (35)	50 increased to 300 max	NR	Placebo (29)	1 tablet	NR	10 weeks	10 weeks	HARS	Imipramine significantly better than placebo in reducing anxiety
	Sabine et al. [94]	United Kingdom	RCT	BN (36)	NA	Mianserin (14)	30 increased to 60 after 1 week	NR	Placebo (22)	NR	NR	8 weeks	8 weeks	HRS-A	Significant decrease in anxiety in both groups, but no significant difference between groups
	Solyom et al. [100]	Canada	Open label	BN (10)	OCD (4)	Fluoxetine (10)	80	NR	NA	NA	NA	3 months	3 months	STAI	Significantly reduced trait anxiety, but not state.
	Walsh [119]	USA	RCT	BN (50)	NR	Phenelzine (23)	60, increased to 90 based on response	NR	Placebo (27)	60, increased to 90 based on response	NR	8 weeks	8 weeks	SCL−90	No significant difference in anxiety or phobic anxiety between groups.
Binge Eating Disorder															
	Calandra et al. [19]	Italy	Cohort	BED (30)	NA	Bupropion (15)	150	33.4 (6.1)	Sertraline (15)	200	32.9 (3.1)	24 weeks	24 weeks	STAI-X	Both significantly reduced anxious symptoms, but no difference between groups
	Carbone et al. [20]	Italy	Open label trial	Obese BED (19) Obese non-BED (15)	NR	Naltrexone and Bupropion BED (19)	8 n 90 b Increased from 1 dose per day to 2	39 (7.8)	Naltrexone and Bupropion non-BED (15)	8 n 90 b Increased from 1 dose per day to 2	43.8 (9.6)	16 weeks	16 weeks	STAI	No significant change in anxiety in BED patients

(*continued on next page*)

Table 2 (*continued*)

	Study Reference	Country	Study Design	ED (N)	Comorbid Anxiety (N)	Drug Agent (N)	Dose mg/ day (m/sd)	BMI m(sd)	Comparator Comparator (N)	Dose mg/ day (m/sd)	BMI m(sd)	Treatment Length	Follow-Up	Anxiety Measure	Results
	Grant et al. [39]	USA	RCT	BED (67)	NR	Vortioxetine (33)	10, increased to 20	39.3	Placebo (34)	NR	36.5	12 weeks	12 weeks	HAM-A	No significant change in anxiety
	Guerdjikova et al. [43]	USA	RCT	BED (40)	Anxiety disorders (12)	Duloxetine (20)	78.7 (19.6)	38.7 (6.8)	Placebo (20)	80.3 (25.2)	42.8 (7.7)	12 weeks	12 weeks	HAM-A	No significant difference between groups in anxiety reduction
	Ricca et al. [89]	Italy	RCT	BED (108)*	OCD (2) Panic Disorder (2)	Fluoxetine (21)	60	32.1 (3.8)	Fluvoxamine (22)	300	32.7 (4.1)	24 weeks	24 weeks 1 year after end	STAI	After 24 weeks of treatment, significant reduction of anxiety in fluvoxamine group, but not fluoxetine[a] 1 year after treatment ended, STAI-1 scores had significantly increased in fluoxetine group[b]
Avoidant Restrictive Food Intake Disorder															
	Gray et al. [41]	USA	Retrospective chart review	ARFID (14)	13 had at least 1 of GAD, SAD, unspecified anxiety disorder, ADHD, MDD.	Mirtazapine monotherapy (6) Mirtazapine with adjunct medication (8)	25 (17.9)	16.8 (5.1)	NA	NA	NA	9.8 weeks (5.1)	NR	NR	Initial anxiety increased resolved with a decreased dosage
	Tanıdır and Hergüner, [106]	Turkey	Case report	ARFID (1)	OCD, a history of separation anxiety disorder, specific phobia	Mirtazapine	15	NR	NA	NA	NA	6 months	6 months	NR	Less mealtime anxiety at 2-weeks that was sustained at 6 months

Notes. *Remaining participants were assigned to other comparative groups of drug+ therapy which are not included in this systematic review. Abbreviations: ADHD = Attention-Deficit/ Hyperactivity Disorder; AN = Anorexia Nervosa; AN-BP = Anorexia Nervosa Binge Purge; AN-R = Anorexia Nervosa Restrictive; ARFID = Avoidant Restrictive Food Intake Disorder; BAI = Beck Anxiety Inventory; BED = Binge Eating Disorder; BN = Bulimia Nervosa; BNnp = Bulimia Nervosa no purge; BNp = Bulimia nervosa purge; EDNOS-bp = Eating Disorder Not Otherwise Specified- Binge Purge; GAD = Generalised Anxiety Disorder; HAM-A = Hamilton Anxiety Rating Scale; HARS = Hamilton Anxiety Rating Scale; ; HRS-A = Hamilton Rating Scale for Anxiety; HSCL = Hopkins Symptom Checklist; MDD = Major Depressive Disorder; NA = Not Applicable; NR = Not Reported; OCD = Obsessive Compulsive Disorder; RCT = Randomised Controlled Trial; SCARED = Self-report for Childhood Anxiety Related Disorders; SAD = Social Anxiety Disorder; SCL = Symptom Checklist; STAI = State Trait Anxiety Inventory; STAI-X = State Trait Anxiety Inventory-X.

Table 3
Characteristics of included studies testing antipsychotic medication.

	Study Reference	Country	Study Design	ED (N)	Comorbid Anxiety Disorder (N)	Drug Agent (N)	Dose mg/day (m/sd)	BMI m(sd)	Comparator Agent (N)	Dose mg/day (m/sd)	BMI m(sd)	Treatment Length	Follow-Up	Anxiety Measure	Results
Anorexia Nervosa															
	Attia et al. [3]	USA	RCT	AN (23)	NR	Olanzapine (11)	2.5, increased to 5 and 10	16.7 (1.5)	Placebo (12)	2.5. increased to 5 and 10	17.4 (1.0)	8 weeks	8 weeks	BAI	No significant difference in anxiety reduction between groups
	Barbarich et al. [6]	USA	Open trial	ANr (12) AN-BP (5)	NR	Olanzapine (17)	2.5–7.5	NR	NA	NA	NA	6 weeks	6 weeks	STAI	Significant improvement in state anxiety
	Boachie et al. [12]	Canada	Case report	AN (4)	OCD (2) Anxiety (1)	Olanzapine (4)	2.5	Range of 12.2–14.5	NA	NA	NA	Range 2–5 months	NR	NR	Decreased pre-meal anxiety
	Court et al. [24]	Australia	RCT	AN (21)	NR	Quetiapine (10)	Started at 50. Increased by 25 and then 50 until max dose of 400 reached.	16.9 (1.7)	TAU (11)	NA	16.3 (1.8)	12 weeks	12 weeks 12 months	MASQ	Positive effect of quetiapine on anxiety versus TAU but not statistically significant
	Dennis et al. [26]	USA	Case report	AN (5)	Anxiety NOS (1)	Olanzapine (5)	Range of 1.25 – 7.5	16.4 (1.5)	NA	NA	NA	NR	NR	NR	Decreased anxiety around eating
	Hagman et al. [44]	USA	Double-blind placebo pilot	AN (40)	NR	Risperidone (18)	2.5 (1.2)	15.9 (1)	Placebo (22)	3 (1)	16.1 (1.3)	8–9 weeks	4-week intervals	MASC	No significant changes in anxiety
	Malina et al. [64]	USA	Retrospective study	AN (18)	NR	Olanzapine (18)	4.7 (2.4)	NR	NA	NA	NA	17 weeks (20)	NA	Own questionnaire	Subjective reduction in anxiety
	Marzola et al. [68]	Italy	Retrospective chart review	ANr (50) AN-BP (25)	NR	Aripiprazole + SSRI (23) Olanzapine + SSRI (27)	9.13 (6.33) 6.11 (3.27)	14.11 (1.94) 13.57 (1.82)	SSRI (25)	Range 11–10 g (depending on SSRI)	14.11 (1.94)	4.96 weeks (1.62)	34.78 days (9.85)	HAM-A	Anxiety reduction in all groups. Aripiprazole group had the biggest reduction, followed by olanzapine, then SSRI.
	Powers et al. [87]	USA	Open label study	AN (19)	NR	Quetiapine (19)	150–300	16.6	NA	NA	NA	10 weeks	10 weeks	STAI	Significant improvement in anxiety
	Powers et al. [88]	USA	RCT	AN (15)	OCD (8) Specific phobia (8) Social phobia (7) GAD (6) Panic disorder (4)[a]	Quetiapine (6)	177.7 (90.8)	15.9 (2.27)	Placebo (9)	NR	15.9 (2.27)	8 weeks	8 Weeks	STAI	No difference in anxiety between groups
	Spettigue, Norris, Maras et al. [101]	Canada	Non-randomised open label trial	AN (32)	NR	Olanzapine (22)	Starting at 1.25–5 and increased by 1.25–2.5. Max dose 15.	16.25 (1.67)	Waitlist (10)	NA	16.76 (0.93)	55 days	12 weeks	MASC	Significant decrease in anxiety, but no difference between groups
	Trunko et al. [115]	USA	Case report	AN (5) BN (3)	OCD (2) GAD (3)	Aripiprazole (8)	Range of 5–15	Range of 14–17 for	NA	NA	NA	Range 3–18 months for	NR	NR	Remission of residual anxiety in

(*continued on next page*)

Table 3 (*continued*)

	Study Reference	Country	Study Design	ED (N)	Comorbid Anxiety Disorder (N)	Drug Agent (N)	Dose mg/day (m/sd)	BMI m(sd)	Comparator Agent (N)	Dose mg/day (m/sd)	BMI m(sd)	Treatment Length	Follow-Up	Anxiety Measure	Results
					Anxiety NOS (1) Social phobia (1)			AN, 20–26 for BN				AN Range 17–41 for BN			1 AN participant. Significant decrease in 1 BN patient.
Avoidant Restrictive Food Intake Disorder															
	Brewerton and D'Agostino [16]	USA	Retrosepctive chart review	ARFID (9)	Anxiety disorder (9)	Olanzapine	2.8 (1.47)	15.6 (1.8)	NA	NA	NA	53.4 days (22.4)	Discharge	NR	Subjective significant improvement in anxiety at discharge
	Spettigue, Norris, Santos et al. [102]	Canada	Case series	ARFID (6)	Anxiety (6) OCD (2)	Olanzapine and fluoxetine (5) Olanzapine and fluvoxamine (1)	Olanzapine range 2.5–5 Fluoxetine range 10–40 Fluvoxamine range 25–100	Range 11.8–13.5	NA	NA	NA	Range 3.5–5 months	Range 3.5–6 momths	NR	Decreased anxiety
Post Traumatic Feeding Disorder	Berger-Gross et al. [11]	USA	Case Report	PTFD (3)	Anxiety NOS (3)	Risperidone	Range 0.125–1.5	NR	NA	NA	NA	Approx. 10 weeks	NR	NR	Anxiety improved in all cases

Notes. [a]based on those who signed informed consent, not who were randomised. Abbreviations: AN = Anorexia Nervosa; AN-BP = Anorexia Nervosa Binge Purge; AN-R = Anorexia Nervosa Restrictive; ARFID = Avoidant-Restrictive Food Intake Disorder; BAI = Beck Anxiety Inventory; BN = Bulimia Nervosa; GAD= Generalised Anxiety Disorder; HAM-A = Hamilton Anxiety Rating Scale; MASC = Multidimensional Anxiety Scale for Children; MASQ = Mood and Anxiety Symptom Questionnaire; NA = Not Applicable; NOS = Not Otherwise Specified; NR = Not Reported; OCD = Obsessive-Compulsive Disorder; PTFD = Post Traumatic Feeding Disorder; RCT = Randomised Controlled Trial; STAI = State Trait Anxiety Inventory.

anxiety reduction after 12 weeks of treatment, as measured by the HAM-A [43].

3.3.6. Reboxetine (SNRI)

3.3.6.1. Reboxetine studies in bulimia nervosa. A pilot study of 28 BN patients given between 2 and 4 mg/day of reboxetine over 12 weeks reported no significant reduction in HAM-A anxiety scores from baseline to 12-weeks [31].

3.3.7. Milnacipran (SNRI)

3.3.7.1. Milnacipran studies in anorexia nervosa and bulimia nervosa. An open label study of Milnacipran in AN-BP (n = 6), BNp (n = 7) and BNnp (n = 7) over eight weeks reported a significant improvement in anxiety on the HAM-A after one week and eight weeks [79].

3.3.8. Phenelzine (MAOI)

3.3.8.1. Phenelzine studies in bulimia nervosa. In 50 BN patients randomised to 60–90 mg/day of phenelzine (n = 23) or placebo (n = 27) for eight weeks, there was no significant difference in anxiety or phobic anxiety measured by the SCL-90 between groups [119].

3.3.9. Vortioxetine (SMS)

3.3.9.1. Vortioxetine studies in binge eating disorder. A double-blind, placebo-controlled study of 67 BED patients receiving either vortioxetine (n = 33; 10 mg/day increased to 20 mg/day) or placebo (n = 34) over 12-weeks showed no significant change in anxiety measured by the HAM-A [39].

3.3.10. Bupropion (Atypical Antidepressant)

3.3.10.1. Bupropion in anorexia nervosa and bulimia nervosa. Bupropion is a noradrenaline-dopamine reuptake inhibitor (NDRI) that is FDA-approved for the treatment of major depressive disorder (MDD) and can be used in other health-related problems including smoking cessation [8]. However, bupropion is contraindicated for people with EDs characterised by purging behaviours due to an increased risk of seizures [53] and exacerbation of pre-existing gastrointestinal and cardiovascular symptoms [67]. An early multicentre controlled trial of bupropion in BN patients by Horne and colleagues [51] documented high frequency of mal grand seizures in some participants and recommended not to administer bupropion to BN patients. Therefore, bupropion has not been tested in AN and is not recommended for these EDs.

3.3.10.2. Bupropion studies in binge eating disorder. A recent open-label trial of naltrexone and bupropion for 16 weeks in 19 obese BED patients reported no significant changes in anxiety on the STAI [20]. A study comparing 150 mg/day of bupropion (n = 15) with 200 mg/day of sertraline (n = 15) in BED patients evidenced that both drugs resulted in significant reduction of anxious symptoms as measured by the STAI-X, but there were no differences between groups [19]. Both drugs induced weight loss, which bupropion showed superior efficacy for [19]. This study suggests that the treatment of BED with anxiety may be best targeted by bupropion due to its similar efficacy in reducing anxiety, symptoms and better efficacy in reducing weight.

3.3.11. Mianserin (Tetracyclic)

3.3.11.1. Mianserin studies in bulimia nervosa. In a double-blind RCT, 36 BN patients were randomised to either 30–60 mg/day of Mianserin (n = 14) or placebo (n = 22), for eight weeks; there was a significant decrease in anxiety on the HRS-A in both groups, but no significant difference between groups [94].

3.3.12. Mirtazapine (Tetracyclic)

3.3.12.1. Mirtazapine studies in avoidant-restrictive food intake disorder. A retrospective chart review of 14 patients with ARFID, 13 of which had at least one comorbid psychiatric disorder (including GAD, SAD, unspecified anxiety disorder, or others), given mirtazapine (m = 25.5, sd = 17.9) either as a monotherapy (n = 6) or in conjunction with additional pharmacotherapy (n = 8) reported initial increased anxiety [41]. In two of these cases, decreasing the mirtazapine dosage from 15 mg and 30 mg per day to 7.5 mg and 15 mg resolved this. A case report of an adolescent with ARIFD and comorbid OCD documented a rapid response to 15 mg of liquid form mirtazapine per day. The patient reported less anxiety at mealtimes at the two-week follow up, and this was sustained at six months [106].

3.3.13. Imipramine (Tricyclic)

3.3.13.1. Imipramine studies in bulimia nervosa. An RCT of BN patients on imipramine (n = 35) or placebo (n = 29) for 10 weeks documented that imipramine was significantly better at reducing anxiety than placebo, as measured by the HARS [72].

3.4. Antipsychotics

Characteristics of included studies can be seen in Table 3.

3.4.1. Olanzapine

3.4.1.1. Olanzapine studies in anorexia nervosa. An open label study of olanzapine (n = 22) versus waitlist (n = 10) in 32 adolescent AN patients reported a significant decrease in anxiety as measured by the MASC, but no significant difference between groups [101]. An RCT by Attia and colleagues [3] of olanzapine (n = 11) versus placebo (n = 12) over eight weeks documented no significant difference in anxiety reduction between groups as measured by the BAI. An open trial of between 2.5 and 7.5 mg/day of olanzapine (n = 17) in ANr (n = 12) and AN-BP (n = 5) patients over six weeks documented significant improvement in state anxiety as measured by the STAI [6].

Additionally, 18 AN patients highlighted significant reductions in anxiety when questioned about their experience on olanzapine (m = 4.7 mg/day, sd = 2.4), for an average of 17 weeks [64].

There is evidence for the use of olanzapine in reducing anxious symptoms in AN patients from case reports documenting decreased pre-meal anxiety [12] and anxiety around eating [26]. These case reports used doses of 2.5 mg/day and 1.25–7.5 mg/day respectively and did not report the measure of anxiety used.

3.4.1.2. Olanzapine studies in avoidant-restrictive food intake disorder. In a case series of six patients with ARFID and co-occurring anxiety disorders treated with olanzapine and either fluoxetine (n = 5) or fluvoxamine (n = 1) reported decreased anxiety [102].

Nine ARFID patients with current comorbid anxiety disorders reported subjective significant improvement in anxiety symptoms at discharge, following an average of 53.4 days of 0.625 mg/day of olanzapine adjunct with a residential and partial hospital ED program [16].

3.4.2. Quetiapine

3.4.2.1. Quetiapine studies in anorexia nervosa. A double-blind placebo-controlled randomised trial in 15 AN patients reported no significant difference in anxiety measured by the STAI between quetiapine (n = 6) and placebo (n = 9) after eight weeks [88].

Contrastingly, one pilot open-label RCT of 400 mg/day of quetiapine

Table 4
Characteristics of included studies testing anxiolytic medication.

	Study Reference	Country	Study Design	ED(N)	Comorbid Anxiety (N)	Drug Agent (N)	Dose mg/day (m/sd)	BMI m (sd)	Comparator Comparator (N)	Dose mg/day (m/sd)	BMI m (sd)	Treatment Length	Follow-Up	Anxiety Measure	Results
Anorexia Nervosa															
	Steinglass et al. [103]	USA	Crossover RCT	AN (20)	Anxiety disorders (5)	Alprazolam (20)	0.75	18 (0.6)	Placebo (20)	0.75	18 (0.6)	2 single dose days 1 week apart	Same days as dosing	STAI-S	No significant reduction, and no difference compared to placebo
Avoidant Restrictive Food Intake Disorder															
	Okereke [80]	USA	Case report	ARFID (1)	NR	Buspirone	10 increased to 20	20.3	NA	NA	NA	8 months	8 months	NR	Initial anxiety decrease at 1 and 2 months, which increased at 6 months and stabilised at 8 months

Abbreviations. AN = Anorexia Nervosa; ARFID = Avoidant Restrictive Food Intake Disorder; NA = Not Applicable; NR = Not Reported; RCT = Randomised Controlled Trial; STAI-S = Spielberger State-Trait Anxiety Inventory- State version.

(n = 10) versus treatment as usual (TAU; n = 11) for 12 weeks in 21 AN patients provides nominal evidence of a positive, but not significant, effect of quetiapine on anxiety measured by the MASQ versus TAU [24]. An open-label trial of 19 AN patients treating with 150–300 mg/day of quetiapine over a 10-week period evidenced improvements in anxiety on the STAI, alongside modest weight gain [87].

3.4.3. Aripiprazole

3.4.3.1. Aripiprazole studies in anorexia nervosa and bulimia nervosa. A retrospective chart review by Marzola and collegagues [68] of 50 ANr and 25 AN-BP patients reported that patients receiving an average of 9. l3 mg/day of aripiprazole plus SSRIs (n = 23) had a greater reduction in anxiety on the HAM-A than patients on SSRIs alone (n = 25). Patients being treated with an average of 6.11 mg/day of olanzapine plus SSRIs (n = 27) also had a greater reduction in anxiety than patients on SSRIs alone. The aripiprazole plus SSRI group had greater anxiety reductions than the olanzapine plus SSRI group [68].

A case report of five AN patients receiving between 5 and 10 mg/day of aripiprazole for between three and 18 months reported remission of residual anxiety in one patient [115]. In the same case series, three BN patients receiving between 7.5 and 15 mg of aripiprazole over a course of between 17 and 41 months reported significant decrease in anxiety for one patient, and notable decreased in anxiety when eating in another [115].

3.4.4. Risperidone

3.4.4.1. Risperidone studies in anorexia nervosa. A double-blind placebo-controlled pilot study of 40 AN patients of risperidone (n = 18) versus placebo (n = 22) for an average of 8.6 and 9.3 weeks respectively, documented no significant changes in anxiety on the MASC over time in either group [44].

3.4.4.2. Risperidone studies in post traumatic feeding disorder. A case report of three patients with Post Traumatic Feeding Disorder (PTFD) and comorbid anxiety disorder not otherwise specified were treated with risperidone (range = 0.125–1.5 mg/day) for approximately 10 weeks, reporting improved anxiety in all cases [11].

3.5. Anxiolytics

Characteristics of included studies can be seen in Table 4.

3.5.1. Alprazolam

3.5.1.1. Alprazolam studies in anorexia nervosa. A randomised double-blind placebo cross-over study in 20 AN patients investigated the use of a single 0.75 mg dose of benzodiazepine alprazolam in treating pre-meal anxiety symptoms using the STAI-S, documenting no significant reduction, and no difference compared to placebo [103].

3.5.2. Buspirone

3.5.2.1. Buspirone studies in avoidant restrictive food intake disorder. One case report of an adolescent female with ARFID and anxiety symptoms treated with buspirone (10 mg/day increased to 20 mg/day) reported an initial decrease in anxiety at one and two months, but increased at six months, and stabilised by month eight [80].

3.6. Anti-convulsants

Characteristics of included studies can be seen in Table 5.

Table 5
Characteristics of included studies testing anticonvulsant medication.

	Study Reference	Country	Study Design	ED(N)	Comorbid Anxiety (N)	Drug Agent (N)	Dose mg/day (m/sd)	BMI m(sd)	Comparator Comparator (N)	Dose mg/ day (m/sd)	BMI m(sd)	Treatment Length	Follow-Up	Anxiety Measure	Results
Bulimia Nervosa															
	Barbee [7]	USA	Case series	BN (5)	Severe affective and/ or anxiety (5)	Topiramate (5)	Range 25–400	NR	NA	NA	NA	Up to 1 year	Up to 18 months	NR	1 case had increased anxiety in the first 4 weeks.
	Bruno et al. [17]	Italy	Case report	BN (1)	OCD (1)	Topiramate Aripiprazole	5 200	45	NA	NA	NA	2 years	2 years	HAM-A	Reduction in anxiety at 1 year and 2 year
	Felstrom and Blackshaw [32]		Case study	BN (1)	NR	Topiramate	75	26	NA	NA	NA	7 months	3 months	NR	Reduced anxiety

Abbreviations. BN = Bulimia Nervosa; HAM-A = Hamilton Anxiety Scale; NA = Not Applicable; NR = Not Reported; OCD = Obsessive-compulsive disorder.

3.6.1. Topiramate

3.6.1.1. Topiramate studies in bulimia nervosa. A case report of one BN patient treated with topiramate (5 mg/day) and aripiprazole (200 mg/day) evidenced a consistent reduction in anxiety symptoms on the HAM-A from baseline to two year follow up [17]. Similarly, a case study of one BN patient treated with 75 mg/day of topiramate for seven months showed reduced anxiety at three months [32].

Contrastingly, an early case series of five BN patients, all with severe comorbid affective and/ or anxiety disorders, were treated with between 25 and 400 mg of topiramate for up to one year [7]. One patient in this case series documented increased anxiety within the first four weeks; anxiety was not reported for other patients [7].

3.7. Stimulants

Characteristics of included studies can be seen in Table 6.

3.7.1. Lisdexamfetamine

3.7.1.1. Lisdexamfetamine studies in binge eating disorder. Lisdexamfetamine (LDX) is FDA-approved for BED with research evidencing its efficacy and safety in the population [36,52,69,76]. However, an open-label trial of LDX in 41 BED patients, five with comorbid anxiety disorders, reported no significant changes in anxiety severity as measured by the HAM-A following eight weeks of either 50 or 70 mg/day of LDX [42].

4. Pharmacological treatments in development

Characteristics of included studies can be seen in Table 7.

4.1. Psilocybin

Psilocybin is a hallucinogenic and psychedelic agent with mechanistic actions via serotonin pathways (5-HT) and high affinity for serotonergic receptors, specifically 5-HT2a [25]. Research into the use of psilocybin in depression populations evidences its antidepressant and anxiolytic properties, indicating potential to ameliorate underlying comorbid disorders, such as anxiety and depression [21,27,63].

An open label feasibility study of a single 25/mg dose of psilocybin in 10 AN patients with a mean BMI of 19.7 evidenced significant reductions of trait anxiety and trait body image anxiety after one month [85]. Trials for psilocybin in BED and AN are ongoing. These trials typically have small sample sizes and results should be considered preliminary, with new and ongoing studies necessary to demonstrate efficacy. Preliminary post-hoc analyses on psilocybin data from ten studies (n = 288) showed no impact of body weight on subjective drug effects and adverse events [34]. Study samples included healthy volunteers, people with major depressive disorder, and cigarette smokers, although no patients with eating disorders or low BMI were included in this analysis. More recent research suggests use of dose escalation or conservative dose strategies in severely ill anorexia nervosa patients [28].

4.1.1. Adverse effects

Common side effects of psilocybin, such as increased blood pressure and heart rate, may worsen existing abnormalities in patients with AN. However, Peck and colleagues [85] showed no significant changes to heart rate or blood pressure from a 25 mg dose in AN patients. Hypoglycaemia is common in AN due to food restriction, which can be exacerbated with psilocybin; Peck and colleagues [85] documented that two participants experienced hypoglycaemia which subsided within 24 hours. It should be considered that this evidence comes from one trial with a small sample size that had a high mean BMI that is not reflective of characteristic severe low weight seen in AN patients. Additionally,

Table 6
Characteristics of included studies testing stimulants.

	Study Reference	Country	Study Design	ED (N)	Comorbid Anxiety (N)	Drug Agent (N)	Dose mg/day (m/sd)	BMI m (sd)	Comparator Comparator (N)	Dose mg/day (m/sd)	BMI m(sd)	Treatment Length	Follow-Up	Anxiety Measure	Results
Binge Eating Disorder	Griffiths et al. [42]	Australia	Open label trial	BED (41)	Anxiety Disorder (5)	LDX (41)	Titrated to 50 or 70	Range from 19 to 40	NA	NA	NA	8 weeks	8 weeks	HAM-A	No significant change in anxiety

Abbreviations. BED = Binge Eating Disorder; HAM-A = Hamilton Anxiety Scale; LDX = Lisdexamfetamine; NA = Not applicable.

this study did not explicitly explore the pharmacokinetic properties of psilocybin.

4.2. Ketamine

Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist that induces synaptic plasticity [47]. The majority of psychiatric research in ketamine focuses on depressive disorders, but recent evidence has documented anxiolytic effects of ketamine, with positive outcomes for GAD, SAD and OCD samples [45,117]. A meta-analysis showed superiority of ketamine versus placebo on anxiety outcomes in studies measuring acute (<12 hour), subacute (24 hours), and sustained (7–14 days) time point effects [45]. This meta-analysis included a range of study samples, including affective disorders, PTSD, OCD and SAD, but not eating disorders.

One case series of four severe-enduring ED (AN-R = 2, EDNOS-bp = 2) patients who were given 0.5 mg/kg of ketamine reported improved anxiety [99]. Another case series of one BN and four AN patients given between 25 and 100 mg doses over 4 sessions, reported two patients with clinically significant improvement in anxiety, with others showing modest but not significant improvements [92]. Similarly, a case report of two AN and one ED with binging purging and restriction were given ketamine by two routes of administration, sublingual or intramuscular [123]. Using the HAM-A, anxiety scores reduced in all three cases following 12 months of ketamine treatment [123].

4.2.1. Adverse effects

Liver injury and hepatotoxicity is associated with repeated high doses or prolonged administration of ketamine; as AN patients are at risk of abnormalities in liver enzymes due to having a low BMI, liver function tests are a necessary prerequisite before beginning ketamine treatment [59]. Additionally, there is a dose-response relationship between ketamine administration and urinary tract symptoms; AN patients often experience renal complications, so monitoring of renal function indicators in the blood should be carried out throughout treatment, with abnormalities meriting cessation of ketamine [59].

4.3. Cannabinoids

A pilot open label uncontrolled study of Δ9-THC in nine AN patients reported no significant changes in anxiety symptoms, although significant improvements were documented in other psychological symptoms including depression [4]. A clinical trial investigating the use of cannabinoids in treatments of meal-time anxiety in anorexia nervosa is underway [65].

5. Discussion

This systematic review has summarised the evidence base for pharmacological agents in treating anxiety symptoms in people with AN, BN, BED, and ARFID. Based on the research presented, the evidence has been graded using the WFSBP guidelines [46]; see Table 8. In summary, there is limited evidence investigating medications to improve anxiety symptoms in ED populations.

This systematic review demonstrated evidence of fluoxetine for anxiety in AN and BN, but not in BED. However, evidence for the use of fluoxetine in AN is mostly demonstrated in weight-restored individuals [67]. In this systematic review, one study included weight-restored AN-R patients [58], and another included patients with a BMI above 19 [120]. Fluoxetine may only be effective in treating comorbid anxiety symptoms following weight restoration due to the change of serotonin activity that is associated with weight gain [58]. This indicates that fluoxetine may be better utilised to help weight recovered AN patients maintain a healthy body weight and improve anxiety symptoms. This is furthered by studies that included AN participants with lower BMIs with no reduction in anxiety [90] or reductions in anxiety that were not

Table 7
Characteristics of included studies on typical and atypical psychedelics and cannabinoids.

	Study Reference	Country	Study Design	ED (N)	Comorbid Anxiety (N)	Drug Agent (N)	Dose mg/day (m/sd)	BMI m (sd)	Comparator Comparator (N)	Dose mg/day (m/sd)	BMI m (sd)	Treatment Length	Follow-Up	Anxiety Measure	Results
Anorexia Nervosa															
	Avraham et al. [4]	Israel	Open label trial	AN (9)	NR	Δ9-THC (9)	1 increased to 2	16.1 (1.6)	NA	NA	NA	4 weeks	4 weeks	STAI	No significant change in anxiety symptoms
	Peck et al. [85]	USA	Open label study	AN (10)	OCD (3) GAD (7)	Psilocybin (10)	25	19.7 (3.7)	NA	NA	NA	Single dose	1 month	STAI-T PASTAS	Significant reductions in anxiety at 1 month.
	Robison et al. [92]	USA	Case series	AN-R (3) AN-BP (1) BN (1)	GAD (3)	Ketamine (5)	Range 25–100	NR	NA	NA	NA	4 weeks	24 hours after final dose	GAD−7	2 showed significant reductions, others showed modest but not significant reduction.
	Schwartz et al. [99]	USA	Case series	AN-R (2) EDNOS-bp (2)	NA	Ketamine (4)	0.5 mg/kg	Range 17.5–37.8	NA	NA	NA	Range 6–18 months	24-hours, 3- and 7-days post-injection	STAI	Improved anxiety, some partially or fully sustained
	Wolfson et al. [123]	USA	Case report	AN (2) ED with binge purge restriction (1)	Panic disorder (1) Anxiety (1) OCD (1)	Ketamine	Various	NR	NA	NA	NA	12 months	12 months	HAM-A	Anxiety reductions in all cases

Abbreviations. AN = Anorexia Nervosa; AN-BP = Anorexia Nervosa binge purge; ANr= Anorexia Nervosa restrictive; BN = Bulimia Nervosa; EDNOS = Eating Disorder not otherwise specified; GAD = Generalised Anxiety Disorder; GAD-7 = Generalised Anxiety Disorder Scale- 7; HAM-A = Hamilton Anxiety Scale; NA = Not Applicable; NR = Not Reported ;OCD = Obsessive-compulsive disorder; PASTAS = Physical Appearance State and Trait Anxiety; STAI = State Trait Anxiety Inventory; STAI-T = Spielberger State-Trait Anxiety Inventory- Trait version; Δ9-THC = delta-9-tetrahydrocannabinol.

Table 8
Level of evidence and grade of recommendation of the pharmacological treatment of anxiety in eating disorders.

Drug Type		Anorexia Nervosa		Bulimia Nervosa		Binge Eating Disorder		Avoidant Restrictive Food Intake Disorder		Post Traumatic Feeding Disorder	
		LoE	GoR	LoE	GoR	GoR	LoE	LoE	GoR	LoE	GoR
Antidepressants											
SSRI	Fluoxetine	B	2	B	2	B-	2-	NSA	NSA	NSA	NSA
	Fluvoxamine	NSA	NSA	B-	2-	NSA	NSA	NSA	NSA	NSA	NSA
	Sertraline	C1-	3-	NSA	NSA	NSA	NSA	NSA	NSA	NSA	NSA
	Vortioxetine	NSA	NSA	NSA	NSA	B-	2-	NSA	NSA	NSA	NSA
	Citalopram	B	2	NSA	NSA	NSA	NSA	NSA	NSA	NSA	NSA
SNRI	Duloxetine	NSA	NSA	C2	3	B-	2-	NSA	NSA	NSA	NSA
	Reboxetine	NSA	NSA	C1-	3-	NSA	NSA	NSA	NSA	NSA	NSA
	Milnacipran	C1	3	C1	3	NSA	NSA	NSA	NSA	NSA	NSA
MAOI	Phenelzine	NSA	NSA	B-	2-	NSA	NSA	NSA	NSA	NSA	NSA
Atypical	Bupropion	D	4	D	4	C1-	3-	NSA	NSA	NSA	NSA
Tetracyclic	Mirtazapine	NSA	NSA	NSA	NSA	NSA	NSA	C2	3	NSA	NSA
	Mianserin	NSA	NSA	B-	2-	NSA	NSA	NSA	NSA	NSA	NSA
Tricyclic	Imipramine	NSA	NSA	B	2	NSA	NSA	NSA	NSA	NSA	NSA
Antipsychotics											
SGA	Olanzapine	B	2	NSA	NSA	NSA	NSA	C2	3	NSA	NSA
	Quetiapine	B	2	NSA	NSA	NSA	NSA	NSA	NSA	NSA	NSA
	Aripiprazole	C2	3	C2	3	NSA	NSA	NSA	NSA	NSA	NSA
	Risperidone	B-	1-	NSA	NSA	NSA	NSA	NSA	NSA	C2	3
Anxiolytics											
Benzodiazepine	Alprazolam	B-	2-	NSA	NSA	NSA	NSA	NSA	NSA	NSA	NSA
Azapirone	Buspirone	NSA	NSA	NSA	NSA	NSA	NSA	C2	3	NSA	NSA
Anti-convulsants	Topiramate	NSA	NSA	C2	3	NSA	NSA	NSA	NSA	NSA	NSA
Stimulants	Lisdexamfetamine	NSA	NSA	NSA	NSA	C1-	3-	NSA	NSA	NSA	NSA
Psychedelics and Cannabinoids	Ketamine	C2	3	NSA	NSA	NSA	NSA	NSA	NSA	NSA	NSA
	Psilocybin	C2	3	NSA	NSA	NSA	NSA	NSA	NSA	NSA	NSA
	Cannabinoids	C2-	3-	NSA	NSA	NSA	NSA	NSA	NSA	NSA	NSA

Notes. NSA = no studies available; Level of evidence (LoE): A = strong evidence that the intervention is effective; B = limited evidence that the intervention is effective; C(1−3) = low evidence that the intervention is effective; −A = Strong evidence that the intervention is NOT effective; −B = Limited evidence that the intervention is NOT effective; −C(1–3)= Low evidence that the intervention is NOT effective; D = no evidence. Grade of recommendation (GoR): 1 = Strong recommendation for using the intervention; 2 = Limited recommendation for using the intervention; 3 = Weak recommendation for using the intervention; −1 = Strong recommendation AGAINST using the intervention; −2 = Limited recommendation AGAINST using the intervention; −3 = Weak recommendation AGAINST using the intervention; 4 = No recommendation possible.

superior to a comparative drug [14,15].

There is preliminary evidence for mirtazapine in ARFID. Other antidepressant research documented evidence against the use of phenelzine, reboxetine, and fluvoxamine for anxiety in BN, and against the use of vortioxetine, duloxetine, and bupropion for anxiety in BED. We document evidence for the use of olanzapine and quetiapine for anxiety in AN, and preliminary evidence for use of olanzapine for anxiety in ARFID. There was limited evidence for the use of aripiprazole for anxiety in AN and BN.

There was some preliminary evidence for the use of buspirone in ARFID, and against the use of alprazolam for anxiety in AN. These findings are inconsistent with evidence that anxiety can be reduced using alprazolam in other clinical populations and is approved for anxiety disorders [35]. There was no other evidence concerning the use of anti-anxiety medication in treating anxiety in eating disorders. Despite the lack of RCTs investigating the use of anti-anxiety medications for anxiety in EDs, clinicians often use benzodiazepines and/or anxiolytics as temporary treatments for anxious symptoms in ED inpatient settings [110]. This necessitates future research to investigate pharmacological options for treating anxiety in EDs, with recommendations and guidelines to be developed. A recent meta-analysis of azapirones in anxiety disorders provide confirmation of azapirone benefit for GAD in comparison to placebo, but document insufficient evidence for its use in panic disorder and SAD [93]. The significantly lower rate of adverse events compared to benzodiazepines and SRIs contribute to a good tolerability profile of azapirones, which may act as suitable alternatives to current anxiety medication [93]. Research into the use of azapirones to treat anxiety comorbid with EDs is suggested.

Notably, there was some preliminary evidence against the use of LDX for treating anxiety in people with BED, despite being a licensed medication for this population. Due to potential side effects of LDX often mimicking symptoms of anxiety, it may be understandable that the findings did not report reduced anxiety [42].

There is preliminary evidence for the use of psilocybin, and ketamine for anxiety in AN, and against the use of cannabinoids in treating anxiety in AN. However, there was no current evidence for these medications for anxiety in BN, BED, and ARFID.

Collectively, there is limited evidence that has investigated the use of different medications to improve anxiety symptoms in ED populations, with varying rates of successes. In particular, there are limited number of studies in ARFID, due to its only recent official recognition in DSM guidelines, and indeed less for OFSED and EDNOS, despite their high prevalence rates. This necessitates the need for continued research into effective medications for anxiety in people with EDs.

5.1. Limitations and future directions

The nature of the crossover between anxiety and EDs with precursive and reciprocal relationships acts as a limitation of this systematic review. Indeed, there are strong bidirectional correlations between anxiety and ED symptoms [29,114]. This may make determining the direct effect of a medication on anxiety symptoms difficult, as improvements in ED symptoms may mediate the improvement in anxiety, or the converse. Additionally, it is notable that some studies included received additional care, including nutritional counselling [13,14], cognitive behavioural therapy [13,14,89,90,120], family therapy [102], or ED programs [16]. Some studies did not account for the effects of adjunct medications and/or alternative treatment methods on reported anxiety outcomes [13,14,16,90,102]; therefore, group differences may be obscured, and sensitivity to detect medication-specific effects may be weakened. The design of controlled trials that investigate the efficacy of these pharmacological treatments as monotherapies, in addition to their combinations, are

needed [102].

The majority of studies included in this review utilised generic measures of anxiety (STAI, HAM-A, etc.) which measure broad constructs and are not sensitive to specific symptoms that manifest in EDs, such as meal-related anxiety, body image anxiety, or specific contexts where anxiety may present, such as mealtimes and social situations. Therefore, whilst measuring improvement in generic and overall anxiety symptoms, these scales may overlook specific anxiety related to EDs. Considering the importance of anxiety in eating behaviours, and its potential role as a causal and/or maintenance factor [121], future research should utilise measures that capture anxiety-eliciting foods and situations, such as the Eating and Anxiety questionnaire [121].

Another limitation of this systematic review is the methodological heterogeneity across included studies. Sample size varied greatly across study designs, ranging from one to 93. Similarly, how ED and comorbid diagnoses were determined differed across studies, including use of The Structured Clinical Interview for DSM-5 and The Mini-International Neuropsychiatric Interview; some studies did not report this information. Additionally, there is relative heterogeneity of BMI of AN samples in studies that focus on moderate weight or weight restored individuals, meaning that conclusions cannot be extrapolated to patients with severely low weight. Low BMI can affect drug efficacy through medical complications, such as renal or hepatic impairment, that vary according to the degree of weight loss [40]. The integration of therapeutic drug monitoring in ED populations may help to ensure safe and effective use of pharmacological treatments for anxiety in EDs.

Therapeutic drug monitoring (TDM) can help to determine effective and safe medication dosages using individual samples and considering individual variability [84,86]. AN patients are characterised by a low BMI and abnormal metabolic profile, which can result in alterations in drug absorption, distribution, and metabolism, thereby affecting individual response to drugs [83,86]. Currently, there is little use of TDM in the ED population, despite a clear indication for its use, and a lack of dosing ranges for underweight patients [86]. To date, only one study [55] has investigated TDM in olanzapine in adolescent AN patients being compliant with all quality criteria. Karwautz and colleagues [55] report a preliminary therapeutic range of olanzapine for adolescent AN patients. Future research should develop TDM studies for current and upcoming pharmacological treatments.

TDM supports the concept of individualised drug treatment, which contributes to a more personalised approach in ED treatment. There is significant heterogeneity within EDs, with as much variability in one person than across persons [62]. Strategies for personalising treatment plans that are tailored to account for individual variability and comorbidities, such as comorbid anxiety, which moderate treatment response, are crucial for identifying effective treatment pathways for individual patients to improve on long-term ED outcomes; therefore, warranting earlier consideration [62,73,111].

In line with implementing a personalised treatment approach, it is important to consider at what stage of illness these medications may be effectively used. Stage of illness models have mainly been conceptualised for AN, but there is little data on stage-oriented treatment [109]. Suggested treatment methods include preventative media literacy and body acceptance in early prodromal stages, family-based therapy in early AN, and psychotherapy and medication in later severe enduring stages [112,113]. Further research into the use and efficacy of these medications at different stages of illness may help with implementation of pharmacological agents into individual treatment plans.

6. Conclusion

This systematic review provided an overview of current and developing pharmacological agents for treating anxiety in EDs. Rates of comorbid anxiety disorders in ED populations are high, and targeting treatment efforts towards anxiety symptoms may help to improve ED outcomes. Future studies are warranted to further determine efficacy of these medications in treating anxiety in ED, and at which stages of illness they may be most useful. These future research efforts may contribute towards implementing personalised treatment approaches.

Use of generative AI: generative AI was not used in this article

Registration and protocol

A protocol was not prepared, and the review was not registered.

Availability of data, code, and other materials

Available upon request

Funding

R.M. is in receipt of a PhD studentship funded by the National Institute for Health and Care Research (NIHR) Maudsley Biomedical Research Centre (BRC). Grant award number: NIHR203318. The views expresses are those of the author and not necessarily those of the NHS, the NIHR, or the Department of Health and Social Care. J.T. and H.H. receive salary support from the National Institute for Health Research (NIHR) Biomedical Research Centre (BRC) at the South London and Maudsley NHS Foundation Trust (SLaM) and Kings College London.

CRediT authorship contribution statement

Rebecca Morris: Writing – review & editing, Writing – original draft, Visualization, Data curation. **Johanna Keeler:** Writing – review & editing, Visualization, Validation, Supervision, Conceptualization. **Janet Treasure:** Writing – review & editing, Validation, Supervision, Conceptualization. **Hubertus Himmerich:** Writing – review & editing, Validation, Supervision, Conceptualization.

Declaration of Competing Interest

H.H., J.L.K., and J.T. report funding from the UK Medical Research Council (MRC) for a double-blinded randomized controlled feasibility trial to test oral ketamine in people with anorexia nervosa and depression; the trial will start in 2025. All other authors declare no conflict of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.phrs.2025.107782.

References

[1] S.E. Altman, S.A. Shankman, What is the association between obsessive-compulsive disorder and eating disorders? Clin. Psychol. Rev. 29 (7) (2009) 638–646, https://doi.org/10.1016/j.cpr.2009.08.001.

[2] American Psychiatric Association, Diagn. Stat. Man. Ment. Disord. Diagn. Stat. Man. Ment. Disord. 5 (5) (2013), https://doi.org/10.1176/appi.books.9780890425596.

[3] E. Attia, A.S. Kaplan, B.T. Walsh, M. Gershkovich, Z. Yilmaz, D. Musante, Y. Wang, Olanzapine versus placebo for out-patients with anorexia nervosa, Psychol. Med. 41 (10) (2011) 2177–2182, https://doi.org/10.1017/s0033291711000390.

[4] Y. Avraham, Y. Latzer, D. Hasid, E. Berry, The impact of Δ9-THC on the psychological symptoms of anorexia nervosa: a pilot study, Isr. J. Psychiatry 54 (2017) 3.

[5] B. Bandelow, C. Allgulander, D.S. Baldwin, D.L. Costa, C. da, D. Denys, N. Dilbaz, K. Domschke, E. Eriksson, N.A. Fineberg, J. Hättenschwiler, E. Hollander, H. Kaiya, T. Karavaeva, S. Kasper, M. Katzman, Y.-K. Kim, T. Inoue, L. Lim, V. Masdrakis, J.M. Menchón, World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for treatment of anxiety, obsessive-compulsive and posttraumatic stress disorders – Version 3. Part I: Anxiety disorders, World J. Biol. Psychiatry 24 (2) (2022) 1–39, https://doi.org/10.1080/15622975.2022.2086295.

[6] N.C. Barbarich, C.W. McConaha, J. Gaskill, M. La Via, G.K. Frank, S. Achenbach, K.H. Plotnicov, W.H. Kaye, An open trial of olanzapine in anorexia nervosa,

J. Clin. Psychiatry 65 (11) (2004) 1480–1482, https://doi.org/10.4088/jcp.v65n1106.
[7] J.G. Barbee, Topiramate in the treatment of severe bulimia nervosa with comorbid mood disorders: a case series, Int. J. Eat. Disord. 33 (4) (2003) 468–472, https://doi.org/10.1002/eat.10154.
[8] S.K. Bardal, J.E. Waechter, D.S. Martin, Chapter 23 - Psychiatry, January 1, in: S. K. Bardal, J.E. Waechter, D.S. Martin (Eds.), ScienceDirect, W.B. Saunders, 2011, ⟨https://www.sciencedirect.com/science/article/abs/pii/B9781437703108000233⟩. January 1.
[9] E.B. Barko, S.M. Moorman, Weighing in: qualitative explorations of weight restoration as recovery in anorexia nervosa, J. Eat. Disord. 11 (1) (2023), https://doi.org/10.1186/s40337-023-00736-9.
[10] A.J. Baxter, K.M. Scott, T. Vos, H.A. Whiteford, Global prevalence of anxiety disorders: a systematic review and meta-regression, Psychol. Med. 43 (05) (2012) 897–910, https://doi.org/10.1017/s003329171200147x.
[11] P. Berger-Gross, D.J. Coletti, K. Hirschkorn, E. Terranova, E.F. Simpser, The effectiveness of risperidone in the treatment of three children with feeding disorders, J. Child Adolesc. Psychopharmacol. 14 (4) (2004) 621–627, https://doi.org/10.1089/cap.2004.14.621.
[12] A. Boachie, G.S. Goldfield, W. Spettigue, Olanzapine use as an adjunctive treatment for hospitalized children with anorexia nervosa: Case reports, Int. J. Eat. Disord. 33 (1) (2002) 98–103, https://doi.org/10.1002/eat.10115.
[13] F. Brambilla, A. Draisci, A. Peirone, M. Brunetta, Combined cognitive-behavioral, psychopharmacological and nutritional therapy in Bulimia nervosa, Neuropsychobiology 32 (2) (1995) 68–71, https://doi.org/10.1159/000119215.
[14] F. Brambilla, A. Draisci, A. Peirone, M. Brunetta, Combined Cognitive-Behavioral, Psychopharmacological and Nutritional Therapy in Eating Disorders, 1. Anorex. Nerv. Restricted Type Neuropsychobiol. 32 (2) (1995) 59–63, https://doi.org/10.1159/000119213.
[15] F. Brambilla, A. Draisci, A. Peirone, M. Brunetta, Combined cognitive-behavioral, psychopharmacological and nutritional therapy in eating disorders, 2. Anorex. Nerv. Binge-Eat. /Purging Type Neuropsychobiology 32 (2) (1995) 64–67, https://doi.org/10.1159/000119214.
[16] T.D. Brewerton, M. D'Agostino, Adjunctive use of olanzapine in the treatment of avoidant restrictive food intake disorder in children and adolescents in an eating disorders program, J. Child Adolesc. Psychopharmacol. 27 (10) (2017) 920–922, https://doi.org/10.1089/cap.2017.0133.
[17] A. Bruno, D. Riganello, A. Marino, Treatment with aripiprazole and topiramate in an obese subject with borderline personality disorder, obsessive-compulsive symptoms and bulimia nervosa: a case report, Cases J. 2 (1) (2009) 7288, https://doi.org/10.4076/1757-1626-2-7288.
[18] S. Byrne, T. Wade, P. Hay, S. Touyz, C.G. Fairburn, J. Treasure, U. Schmidt, V. McIntosh, K. Allen, A. Fursland, R.D. Crosby, A randomised controlled trial of three psychological treatments for anorexia nervosa, Psychol. Med. 47 (16) (2017) 2823–2833, https://doi.org/10.1017/s0033291717001349.
[19] C. Calandra, R.G. Russo, M. Luca, Bupropion versus sertraline in the treatment of depressive patients with binge eating disorder: retrospective cohort study, Psychiatr. Q. 83 (2) (2012) 177–185, https://doi.org/10.1007/s11126-011-9192-0.
[20] E.A. Carbone, M. Caroleo, M. Rania, G. Calabrò, F.A. Staltari, R. de Filippis, M. Aloi, F. Condoleo, F. Arturi, C. Segura-Garcia, An open-label trial on the efficacy and tolerability of naltrexone/bupropion SR for treating altered eating behaviours and weight loss in binge eating disorder, Eat. Weight Disord. - Stud. Anorex., Bulim. Obes. 26 (3) (2021) 779–788, https://doi.org/10.1007/s40519-020-00910-x.
[21] R.L. Carhart-Harris, L. Roseman, M. Bolstridge, L. Demetriou, J.N. Pannekoek, M. B. Wall, M. Tanner, M. Kaelen, J. McGonigle, K. Murphy, R. Leech, H.V. Curran, D.J. Nutt, Psilocybin for treatment-resistant depression: fMRI-measured brain mechanisms, Sci. Rep. 7 (1) (2017), https://doi.org/10.1038/s41598-017-13282-7.
[22] M. Cederlöf, L.M. Thornton, J. Baker, P. Lichtenstein, H. Larsson, C. Rück, C. M. Bulik, D. Mataix-Cols, Etiological overlap between obsessive-compulsive disorder and anorexia nervosa: a longitudinal cohort, multigenerational family and twin study, World Psychiatry 14 (3) (2015) 333–338, https://doi.org/10.1002/wps.20251.
[23] R.C. Christensen, R.N. Averbuch, The use of duloxetine in chronic bulimia nervosa: a case report, Psychiatry (Edgmont) 6 (8) (2009) 27. ⟨https://pmc.ncbi.nlm.nih.gov/articles/PMC2743210/⟩.
[24] A. Court, C. Mulder, M. Kerr, H.P. Yuen, M. Boasman, S. Goldstone, J. Fleming, S. Weigall, H. Derham, C. Huang, P. McGorry, G. Berger, Investigating the effectiveness, safety and tolerability of quetiapine in the treatment of anorexia nervosa in young people: a pilot study, J. Psychiatr. Res. 44 (15) (2010) 1027–1034, https://doi.org/10.1016/j.jpsychires.2010.03.011.
[25] J. Daniel, M. Haberman, Clinical potential of psilocybin as a treatment for mental health conditions, Ment. Health Clin. 7 (1) (2017) 24–28, https://doi.org/10.9740/mhc.2017.01.024.
[26] K. Dennis, D. Le Grange, J. Bremer, Olanzapine use in adolescent anorexia nervosa, Eat. Weight Disord. - Stud. Anorex., Bulim. Obes. 11 (2) (2006) e53–e56, https://doi.org/10.1007/bf03327760.
[27] M.K. Doss, M. Považan, M.D. Rosenberg, N.D. Sepeda, A.K. Davis, P.H. Finan, G. S. Smith, J.J. Pekar, P.B. Barker, R.R. Griffiths, F.S. Barrett, Psilocybin therapy increases cognitive and neural flexibility in patients with major depressive disorder, Transl. Psychiatry 11 (1) (2021) 1–10, https://doi.org/10.1038/s41398-021-01706-y.
[28] A.E. Downey, A.V. Chaphekar, J. Woolley, M. Raymond-Flesch, Psilocybin therapy and anorexia nervosa: a narrative review of safety considerations for researchers and clinicians, J. Eat. Disord. 12 (1) (2024), https://doi.org/10.1186/s40337-024-01005-z.
[29] E. Eriksson, M. Ramklint, M. Wolf-Arehult, M. Isaksson, The relationship between self-control and symptoms of anxiety and depression in patients with eating disorders: a cross-sectional study including exploratory longitudinal data, J. Eat. Disord. 11 (1) (2023), https://doi.org/10.1186/s40337-023-00750-x.
[30] S. Fassino, Efficacy of citalopram in anorexia nervosa: a pilot study, Eur. Neuropsychopharmacol. 12 (5) (2002) 453–459, https://doi.org/10.1016/s0924-977x(02)00058-5.
[31] S. Fassino, G.A. Daga, S. Boggio, L. Garzaro, A. Pierò, Use of Reboxetine in Bulimia Nervosa: A Pilot Study, J. Psychopharmacol. 18 (3) (2004) 423–428, https://doi.org/10.1177/026988110401800314.
[32] A. FELSTROM, S. BLACKSHAW, Topiramate for Bulimia Nervosa With Bipolar II Disorder, Am. J. Psychiatry 159 (7) (2002) 1246-a–1247, https://doi.org/10.1176/appi.ajp.159.7.1246-a.
[33] M. Fichter, C. Leibl, R. Krüger, W. Rief, Effects of Fluvoxamine on Depression, Anxiety, and Other Areas of General Psychopathology in Bulimia Nervosa, Pharmacopsychiatry 30 (03) (1997) 85–92, https://doi.org/10.1055/s-2007-979488.
[34] A. Garcia-Romeu, F.S. Barrett, T.M. Carbonaro, M.W. Johnson, R.R. Griffiths, Optimal dosing for psilocybin pharmacotherapy: considering weight-adjusted and fixed dosing approaches, J. Psychopharmacol. 35 (4) (2021) 353–361, https://doi.org/10.1177/0269881121991822.
[35] T. George, J. Tripp, *Alprazolam*. Nih.gov, April 24, StatPearls Publishing, 2023, ⟨https://www.ncbi.nlm.nih.gov/books/NBK538165/⟩. April 24.
[36] A. Ghaderi, J. Odeberg, S. Gustafsson, M. Rastam, A. Brolund, A. Pettersson, T. Parling, Psychological, pharmacological, and combined treatments for binge eating disorder: a systematic review and meta- analysis, PeerJ (2018).
[37] N.T. Godart, M.F. Flament, Y. Lecrubier, P. Jeammet, Anxiety disorders in anorexia nervosa and bulimia nervosa: co-morbidity and chronology of appearance, Eur. Psychiatry 15 (1) (2000) 38–45, https://doi.org/10.1016/s0924-9338(00)00212-1.
[38] R.D. Goodwin, M.L. Fitzgibbon, Social anxiety as a barrier to treatment for eating disorders, Int. J. Eat. Disord. 32 (1) (2002) 103–106, https://doi.org/10.1002/eat.10051.
[39] J.E. Grant, S. Valle, E. Cavic, S.A. Redden, S.R. Chamberlain, A double-blind, placebo-controlled study of vortioxetine in the treatment of binge-eating disorder, Int. J. Eat. Disord. 52 (7) (2019) 786–794, https://doi.org/10.1002/eat.23078.
[40] G. Gravina, W. Milano, G. Nebbiai, C. Piccione, A. Capasso, Medical Complications in Anorexia and Bulimia Nervosa, Endocr., Metab. Immune Disord. - Drug Targets 18 (5) (2018) 477–488, https://doi.org/10.2174/1871530318666180531094508.
[41] E. Gray, T. Chen, J. Menzel, T. Schwartz, W.H. Kaye, Mirtazapine and Weight Gain in Avoidant and Restrictive Food Intake Disorder, J. Am. Acad. Child Adolesc. Psychiatry 57 (4) (2018) 288–289, https://doi.org/10.1016/j.jaac.2018.01.011.
[42] K.R. Griffiths, S. Boulet, S. Barakat, S. Touyz, P. Hay, S. Maguire, M.R. Kohn, Exploring bi-directional impacts of Lisdexamfetamine dimesylate on psychological comorbidities and quality of life in people with Binge Eating Disorder, J. Eat. Disord. 12 (1) (2024), https://doi.org/10.1186/s40337-024-01041-9.
[43] A.I. Guerdjikova, S.L. McElroy, E.L. Winstanley, E.B. Nelson, N. Mori, J. McCoy, P.E. Keck, J.I. Hudson, Duloxetine in the treatment of binge eating disorder with depressive disorders: A placebo-controlled trial, Int. J. Eat. Disord. 45 (2) (2011) 281–289, https://doi.org/10.1002/eat.20946.
[44] J. Hagman, J. Gralla, E. Sigel, S. Ellert, M. Dodge, R. Gardner, T. O'Lonergan, G. Frank, M.Z. Wamboldt, A double-blind, placebo-controlled study of risperidone for the treatment of adolescents and young adults with anorexia nervosa: a pilot study, J. Am. Acad. Child Adolesc. Psychiatry 50 (9) (2011) 915–924, https://doi.org/10.1016/j.jaac.2011.06.009.
[45] H. Hartland, K. Mahdavi, L.A. Jelen, R. Strawbridge, A.H. Young, L. Alexander, A transdiagnostic systematic review and meta-analysis of ketamine's anxiolytic effects, J. Psychopharmacol. 37 (8) (2023) 764–774, https://doi.org/10.1177/02698811231161627.
[46] A. Hasan, B. Bandelow, L.N. Yatham, M. Berk, P. Falkai, H.-J. Möller, S. Kasper, WFSBP guidelines on how to grade treatment evidence for clinical guideline development, World J. Biol. Psychiatry 20 (1) (2019) 2–16, https://doi.org/10.1080/15622975.2018.1557346.
[47] D.F. Hermens, G. Simcock, M. Dutton, A.P. Bouças, A.T. Can, C. Lilley, J. Lagopoulos, Anorexia nervosa, zinc deficiency and the glutamate system: The ketamine option, Prog. Neuro-Psychopharmacol. Biol. Psychiatry 101 (2020) 109921, https://doi.org/10.1016/j.pnpbp.2020.109921.
[48] H. Himmerich, C. Kan, K. Au, J. Treasure, Pharmacological treatment of eating disorders, comorbid mental health problems, malnutrition and physical health consequences, Pharmacol. Ther. 217 (107667) (2021) 107667, https://doi.org/10.1016/j.pharmthera.2020.107667.
[49] H. Himmerich, Y.D. Lewis, C. Conti, H. Mutwalli, A. Karwautz, J.M. Sjögren, M. M. Uribe Isaza, M. Tyszkiewicz-Nwafor, M. Aigner, S.L. McElroy, J. Treasure, S. Kasper, U. Bailer, C.M. Bulik, C. Conti, M.D. Zwaan, A. Favaro, F. Fernandez-Aranda, S. Fetissov, A. Hilbert, World Federation of Societies of Biological Psychiatry (WFSBP) guidelines update 2023 on the pharmacological treatment of eating disorders, World J. Biol. Psychiatry (2023) 1–64, https://doi.org/10.1080/15622975.2023.2179663.
[50] H. Himmerich, J. Treasure, Psychopharmacological advances in eating disorders, Expert Rev. Clin. Pharmacol. 11 (1) (2018) 95–108, https://doi.org/10.1080/17512433.2018.1383895.

[51] R.L. Horne, J.M. Ferguson, H.G. Pope, J.I. Hudson, C.G. Lineberry, J. Ascher, A. Cato, Treatment of bulimia with bupropion: a multicenter controlled trial, J. Clin. Psychiatry 49 (7) (1988) 262–266. ⟨https://pubmed.ncbi.nlm.nih.gov/3134343/⟩.

[52] J.I. Hudson, S.L. McElroy, M.C. Ferreira-Cornwell, J. Radewonuk, M. Gasior, Efficacy of lisdexamfetamine in adults with moderate to severe binge-eating disorder, JAMA Psychiatry 74 (9) (2017) 903, https://doi.org/10.1001/jamapsychiatry.2017.1889.

[53] M. Israël, Should some drugs be avoided when treating bulimia nervosa? J. Psychiatry Neurosci. 27 (6) (2002) 457. ⟨https://pmc.ncbi.nlm.nih.gov/articles/PMC161720/⟩.

[54] R. Kanerva, A. Rissanen, S. Sarna, Fluoxetine in the treatment of anxiety, depressive symptoms, and eating-related symptoms in bulimia nervosa, Nord. J. Psychiatry 49 (4) (1995) 237–242, https://doi.org/10.3109/08039489509011912.

[55] A. Karwautz, M.D. Zeiler, J. Schwarzenberg, Dunja Mairhofer, M. Mitterer, S. Truttmann, J. Philipp, D. Koubek, M. Glüder, G. Wagner, Agnieszka Malcher, G. Schöfbeck, C. Laczkovics, H. Rock, A. Zanko, Hartmut Imgart, T. Banaschewski, C. Fleischhaker, C.U. Correll, Christoph Wewetzer, Therapeutic drug monitoring in adolescents with anorexia nervosa for safe treatment with adjunct olanzapine, Eur. Eat. Disord. Rev. 32 (2023), https://doi.org/10.1002/erv.3022.

[56] J. Kask, L. Ekselius, L. Brandt, N. Kollia, A. Ekbom, F.C. Papadopoulos, Mortality in Women With Anorexia Nervosa, Psychosom. Med. 78 (8) (2016) 910–919, https://doi.org/10.1097/psy.0000000000000342.

[57] W.H. Kaye, C.M. Bulik, L. Thornton, N. Barbarich, K. Masters, Comorbidity of anxiety disorders with anorexia and bulimia nervosa, Am. J. Psychiatry 161 (12) (2004) 2215–2221, https://doi.org/10.1176/appi.ajp.161.12.2215.

[58] W.H. Kaye, T. Nagata, T.E. Weltzin, L.K. Hsu, M.S. Sokol, C. McConaha, K. H. Plotnicov, J. Weise, D. Deep, Double-blind placebo-controlled administration of fluoxetine in restricting- and restricting-purging-type anorexia nervosa, Biol. Psychiatry 49 (7) (2001) 644–652, https://doi.org/10.1016/s0006-3223(00)01013-1.

[59] J.L. Keeler, J. Treasure, M.F. Juruena, C. Kan, H. Himmerich, Ketamine as a Treatment for Anorexia Nervosa: A Narrative Review, Nutrients 13 (11) (2021) 4158, https://doi.org/10.3390/nu13114158.

[60] J. Kerr-Gaffney, A. Harrison, K. Tchanturia, Social anxiety in the eating disorders: a systematic review and meta-analysis, Psychol. Med. 48 (15) (2018) 2477–2491, https://doi.org/10.1017/s0033291718000752.

[61] L.A. Kotler, M.J. Devlin, M. Davies, B.T. Walsh, An Open Trial of Fluoxetine for Adolescents with Bulimia Nervosa, J. Child Adolesc. Psychopharmacol. 13 (3) (2003) 329–335, https://doi.org/10.1089/104454603322572660.

[62] C.A. Levinson, C. Cusack, R. Hunt, H.F. Fitterman-Harris, C. Ralph-Nearman, S. Hooper, The future of the eating disorder field: Inclusive, aware of systems, and personalized, Behav. Res. Ther. 183 (2024).

[63] H. Lowe, N. Toyang, B. Steele, J. Grant, A. Ali, L. Gordon, W. Ngwa, Psychedelics: alternative and potential therapeutic options for treating mood and anxiety disorders, Molecules 27 (8) (2022) 2520, https://doi.org/10.3390/molecules27082520.

[64] A. Malina, J. Gaskill, C. McConaha, G.K. Frank, M. LaVia, L. Scholar, W.H. Kaye, Olanzapine treatment of anorexia nervosa: a retrospective study, Int. J. Eat. Disord. 33 (2) (2003) 234–237, https://doi.org/10.1002/eat.10122.

[65] K. Mallick, M.F. Khan, S. Banerjee, The anxiolytic effects of cannabinoids: A comprehensive review, Pharmacol. Biochem. Behav. 243 (2024) 173828, https://doi.org/10.1016/j.pbb.2024.173828.

[66] L. Mandelli, S. Draghetti, U. Albert, D. De Ronchi, A.-R. Atti, Rates of comorbid obsessive-compulsive disorder in eating disorders: a meta-analysis of the literature, J. Affect. Disord. 277 (2020) 927–939, https://doi.org/10.1016/j.jad.2020.09.003.

[67] M. Marvanova, K. Gramith, Role of antidepressants in the treatment of adults with anorexia nervosa, Ment. Health Clin. 8 (3) (2018) 127–137, https://doi.org/10.9740/mhc.2018.05.127.

[68] E. Marzola, N. Desedime, C. Giovannone, F. Amianto, S. Fassino, G. Abbate-Daga, Atypical antipsychotics as augmentation therapy in anorexia nervosa, PLOS ONE 10 (4) (2015) e0125569, https://doi.org/10.1371/journal.pone.0125569.

[69] S.L. McElroy, J.I. Hudson, J.E. Mitchell, D. Wilfley, M.C. Ferreira-Cornwell, J. Gao, J. Wang, T. Whitaker, J. Jonas, M. Gasior, Efficacy and safety of lisdexamfetamine for treatment of adults with moderate to severe binge-eating disorder, JAMA Psychiatry 72 (3) (2015) 235, https://doi.org/10.1001/jamapsychiatry.2014.2162.

[70] H. Melles, S. Duijvis, A. Jansen, Inhibitory learning during exposure treatment in anorexia nervosa: a practical guide, Behav. Sci. 13 (5) (2023) 370, https://doi.org/10.3390/bs13050370.

[71] H. Melles, A. Jansen, Anxiety matters: a pilot lab study into food, weight, and virtual body exposure in anorexia nervosa, J. Eat. Disord. 12 (1) (2024), https://doi.org/10.1186/s40337-024-01094-w.

[72] J.E. Mitchell, A comparison study of antidepressants and structured intensive group psychotherapy in the treatment of bulimia nervosa, Arch. Gen. Psychiatry 47 (2) (1990) 149, https://doi.org/10.1001/archpsyc.1990.01810140049008.

[73] D. Moggia, W. Lutz, E.-L. Brakemeier, L. Bickman, Treatment Personalization and Precision Mental Health Care: Where are we and where do we want to go? Adm. Policy Ment. Health Ment. Health Serv. Res. 51 (5) (2024) 611–616, https://doi.org/10.1007/s10488-024-01407-w.

[74] S. Moola, Z. Munn, C. Tufanaru, E. Aromataris, K. Sears, R. Sfectu, M. Currie, R. Qureshi, P. Mattis, K. Lisy, P.-F. Mu, Chapter 7: systematic reviews of ethology and risk, in: E. Aromataris, Z. Munn (Eds.), Joanna Briggs Institute Reviewer's Manual, The Joanna Briggs Institute, 2017.

[75] Z. Munn, T.H. Barker, S. Moola, C. Tufanaru, C. Stern, A. McArthur, M. Stephenson, E. Aromataris, Methodological Quality of Case Series Studies, JBI Database Syst. Rev. Implement. Rep. 18 (10) (2020) 1. ⟨https://pubmed.ncbi.nlm.nih.gov/33038125/⟩.

[76] A.F. Muratore, E. Attia, Psychopharmacologic Management of Eating Disorders, Curr. Psychiatry Rep. 24 (7) (2022) 345–351, https://doi.org/10.1007/s11920-022-01340-5.

[77] S.B. Murray, D.S. Quintana, K.L. Loeb, S. Griffiths, D. Le Grange, Treatment outcomes for anorexia nervosa: a systematic review and meta-analysis of randomized controlled trials, Psychol. Med. 49 (04) (2018) 535–544, https://doi.org/10.1017/s0033291718002088.

[78] National Institute for Health and Care Excellence. (2017, May 23). *Overview | Eating disorders: Recognition and Treatment | Guidance | NICE*. Nice.org.uk; NICE. ⟨https://www.nice.org.uk/guidance/ng69⟩.

[79] S. Noma, Effects of milnacipran on binge eating – a pilot study, Neuropsychiatr. Dis. Treat. (2008) 295, https://doi.org/10.2147/ndt.s2505.

[80] N.K. Okereke, Buspirone treatment of anxiety in an adolescent female with avoidant/restrictive food intake disorder, J. Child Adolesc. Psychopharmacol. 28 (6) (2018) 425–426, https://doi.org/10.1089/cap.2018.0005.

[81] M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, L. Shamseer, J.M. Tetzlaff, E.A. Akl, S.E. Brennan, R. Chou, J. Glanville, J. M. Grimshaw, A. Hróbjartsson, M.M. Lalu, T. Li, E.W. Loder, E. Mayo-Wilson, S. McDonald, L.A. McGuinness, The PRISMA 2020 statement: an Updated Guideline for Reporting Systematic Reviews, Br. Med. J. 372 (71) (2021), https://doi.org/10.1136/bmj.n71.

[82] E. PALLISTER, G. WALLER, Anxiety in the eating disorders: Understanding the overlap, Clin. Psychol. Rev. 28 (3) (2008) 366–386, https://doi.org/10.1016/j.cpr.2007.07.001.

[83] F. Panariello, T. Mastellari, A. di Gianni, M. Speciani, D. De Ronchi, A. Atti, M. Protti, L. Mercolini, Antidepressant Therapeutic Drug Monitoring by Minimally Invasive Techniques in Eating Disorders Patients: Preliminary Results from a Pilot Study with Focus on Vortioxetine, Biomed. J. Sci. Tech. Res. 31 (5) (2020), https://doi.org/10.26717/bjstr.2020.31.005163.

[84] L. Patteet, M. Morrens, K.E. Maudens, P. Niemegeers, B. Sabbe, H. Neels, Therapeutic drug monitoring of common antipsychotics, Ther. Drug Monit. 34 (6) (2012) 629–651, https://doi.org/10.1097/ftd.0b013e3182708ec5.

[85] S.K. Peck, S. Shao, T. Gruen, K. Yang, A. Babakanian, J. Trim, D.M. Finn, W. H. Kaye, Psilocybin therapy for females with anorexia nervosa: a phase 1, open-label feasibility study, Nat. Med. 29 (8) (2023) 1–7, https://doi.org/10.1038/s41591-023-02455-9.

[86] F. Pennazio, C. Brasso, V. Villari, P. Rocca, Current Status of Therapeutic Drug Monitoring in Mental Health Treatment: A Review, 2674–2674, Pharmaceutics 14 (12) (2022), https://doi.org/10.3390/pharmaceutics14122674.

[87] P.S. Powers, Y. Bannon, R. Eubanks, T. McCormick, Quetiapine in anorexia nervosa patients: an open label outpatient pilot study, Int. J. Eat. Disord. 40 (1) (2007) 21–26, https://doi.org/10.1002/eat.20325.

[88] P.S. Powers, M. Klabunde, W. Kaye, Double-blind placebo-controlled trial of quetiapine in anorexia nervosa, Eur. Eat. Disord. Rev. 20 (4) (2012) 331–334, https://doi.org/10.1002/erv.2169.

[89] V. Ricca, E. Mannucci, B. Mezzani, S. Moretti, M. Di Bernardo, M. Bertelli, C. M. Rotella, C. Faravelli, Fluoxetine and fluvoxamine combined with individual cognitive-behaviour therapy in binge eating disorder: a one-year follow-up study, Psychother. Psychosom. 70 (6) (2001) 298–306, https://doi.org/10.1159/000056270.

[90] V. Ricca, E. Mannucci, A. Paionni, M. Di Bernardo, M. Cellini, P.L. Cabras, C. M. Rotella, Venlafaxine versus fluoxetine in the treatment of atypical anorectic outpatients: A preliminary study, Eat. Weight Disord. - Stud. Anorex., Bulim. Obes. 4 (1) (1999) 10–14, https://doi.org/10.1007/bf03341582.

[91] E. Riquin, A. Raynal, L. Mattar, C. Lalanne, F. Hirot, C. Huas, J. Duclos, EVHAN group, S. Berthoz, N. Godart, Is the severity of the clinical expression of anorexia nervosa influenced by an anxiety, depressive, or obsessive-compulsive comorbidity over a lifetime? Front. Psychiatry 12 (2021).

[92] R. Robison, A. Lafrance, M. Brendle, M. Smith, C. Moore, S. Ahuja, S. Richards, N. Hawkins, E. Strahan, A case series of group-based ketamine-assisted psychotherapy for patients in residential treatment for eating disorders with comorbid depression and anxiety disorders, J. Eat. Disord. 10 (1) (2022), https://doi.org/10.1186/s40337-022-00588-9.

[93] F. Rossano, C. Caiazza, N. Zotti, Luca Viacava, Antonella Irano, Niccolò Solini, L. Pistone, R. Pezone, F. Cilmi, C. Ricci, Michele De Prisco, F. Iasevoli, T. Kishi, M. Solmi, Andrea de Bartolomeis, M. Fornaro, The efficacy, safety, and adverse events of azapirones in anxiety disorders: a systematic review and meta-analysis of randomized controlled trials, Eur. Neuropsychopharmacol. 76 (2023) 23–51, https://doi.org/10.1016/j.euroneuro.2023.07.008.

[94] E. Sabine, A. Yonace, A. Farrington, K. Barratt, A. Wakeling, Bulimia nervosa: a placebo controlled double-blind therapeutic trial of mianserin, Br. J. Clin. Pharmacol. 15 (S2) (1983) 195S202S, https://doi.org/10.1111/j.1365-2125.1983.tb05866.x.

[95] M. Sala, A. Keshishian, S. Song, R. Moskowitz, C.M. Bulik, C.R. Roos, C. A. Levinson, Predictors of relapse in eating disorders: a meta-analysis, J. Psychiatr. Res. 158 (2023) 281–299, https://doi.org/10.1016/j.jpsychires.2023.01.002.

[96] P. Santonastaso, S. Friederici, A. Favaro, Sertraline in the treatment of restricting anorexia nervosa: an open controlled trial, J. Child Adolesc. Psychopharmacol. 11 (2) (2001) 143–150, https://doi.org/10.1089/104454601750284045.

[97] K. Schaumberg, S. Zerwas, E. Goodman, Z. Yilmaz, C.M. Bulik, N. Micali, Anxiety disorder symptoms at age 10 predict eating disorder symptoms and diagnoses in adolescence, J. Child Psychol. Psychiatry 60 (6) (2018) 686–696, https://doi.org/10.1111/jcpp.12984.
[98] U. Schmidt, T.D. Wade, J. Treasure, The Maudsley Model of Anorexia Nervosa Treatment for Adults (MANTRA): Development, Key Features, and Preliminary Evidence, J. Cogn. Psychother. 28 (1) (2014) 48–71, https://doi.org/10.1891/0889-8391.28.1.48.
[99] T. Schwartz, M.E. Trunko, D. Feifel, E. Lopez, D. Peterson, G.K.W. Frank, W. Kaye, A longitudinal case series of IM ketamine for patients with severe and enduring eating disorders and comorbid treatment-resistant depression, Clin. Case Rep. 9 (5) (2021), https://doi.org/10.1002/ccr3.3869.
[100] L. SOLYOM, C. SOLYOM, B. LEDWIDGE, The Fluoxetine Treatment of Low-Weight, Chronic Bulimia Nervosa, J. Clin. Psychopharmacol. 10 (6) (1990) 421–425, https://doi.org/10.1097/00004714-199010060-00008.
[101] W. Spettigue, M.L. Norris, D. Maras, N. Obeid, S. Feder, M.E. Harrison, R. Gomez, M.C. Fu, K. Henderson, A. Buchholz, Evaluation of the effectiveness and safety of olanzapine as an adjunctive treatment for anorexia nervosa in adolescents: an open-label trial, J. Can. Acad. Child Adolesc. Psychiatry 27 (3) (2018) 197. ⟨https://pmc.ncbi.nlm.nih.gov/articles/PMC6054282/⟩.
[102] W. Spettigue, M.L. Norris, A. Santos, N. Obeid, Treatment of children and adolescents with avoidant/restrictive food intake disorder: a case series examining the feasibility of family therapy and adjunctive treatments, J. Eat. Disord. 6 (1) (2018), https://doi.org/10.1186/s40337-018-0205-3.
[103] J.E. Steinglass, S.C. Kaplan, Y. Liu, Y. Wang, B.T. Walsh, The (lack of) effect of alprazolam on eating behavior in anorexia nervosa: a preliminary report, Int. J. Eat. Disord. 47 (8) (2014) 901–904, https://doi.org/10.1002/eat.22343.
[104] J. Steinglass, R. Sykso, J. Schebendach, A. Broft, M. Strober, T. Walsh, The application of exposure therapy and D-cycloserine to the treatment of anorexia nervosa: a preliminary trial, J. Psychiatr. Pract. 13 (4) (2007).
[105] J. Swinbourne, C. Hunt, M. Abbott, J. Russell, T. St Clare, S. Touyz, The comorbidity between eating disorders and anxiety disorders: prevalence in an eating disorder sample and anxiety disorder sample, Aust. N. Z. J. Psychiatry 46 (2) (2012) 118–131, https://doi.org/10.1177/0004867411432071.
[106] C. Tanıdır, S. Hergüner, Mirtazapine for choking phobia: report of a pediatric case, J. Child Adolesc. Psychopharmacol. 25 (8) (2015) 659–660, https://doi.org/10.1089/cap.2015.0145.
[107] The EndNote Team. (2013) EndNote (21). [Computer Software Program]. Clarivate.
[108] L.M. Thornton, J.E. Dellava, T.L. Root, P. Lichtenstein, C.M. Bulik, Anorexia nervosa and generalized anxiety disorder: further explorations of the relation between anxiety and body mass index, J. Anxiety Disord. 25 (5) (2011) 727–730, https://doi.org/10.1016/j.janxdis.2011.03.010.
[109] E. Tomba, L. Tecuta, V. Gardini, G. Tomei, E. Lo Dato, Staging models in eating disorders: a systematic scoping review of the literature, 152468–152468, Compr. Psychiatry 131 (2024), https://doi.org/10.1016/j.comppsych.2024.152468.
[110] F. Toppino, M. Martini, P. Longo, I. Caldas, N. Delsedime, R. Lavalle, F. Raimondi, G. Abbate-Daga, Matteo Panero, Inpatient treatments for adults with anorexia nervosa: a systematic review of literature, Eat. Weight Disord. 29 (1) (2024), https://doi.org/10.1007/s40519-024-01665-5.
[111] J. Treasure, Treatment resistance in eating disorders: a question of uncertain targets or insufficient personalization? Int. Rev. Psychiatry 31 (4) (2019) 305–307, https://doi.org/10.1080/09540261.2019.1626142.
[112] J. Treasure, V. Cardi, J. Leppanen, R. Turton, New treatment approaches for severe and enduring eating disorders, Physiol. Behav. 152 (2015) 456–465, https://doi.org/10.1016/j.physbeh.2015.06.007.
[113] J. Treasure, D. Stein, S. Maguire, Has the time come for a staging model to map the course of eating disorders from high risk to severe enduring illness? An examination of the evidence, Early Interv. Psychiatry 9 (3) (2015) 173–184, https://doi.org/10.1111/eip.12170.
[114] N. Trompeter, Ş. Dârvariu, A.V. Brieva-Toloza, M.-C. Opitz, F.D. Rabelo-da-Ponte, H. Sharpe, S. Desrivieres, U. Schmidt, N. Micali, The prospective relationship between anxiety symptoms and eating disorder symptoms among adolescents: a systematic review and meta-analysis of a bi-directional relationship. European Child & Adolescent Psychiatry, 2024, https://doi.org/10.1007/s00787-024-02601-9.
[115] M.E. Trunko, T.A. Schwartz, V. Duvvuri, W.H. Kaye, Aripiprazole in anorexia nervosa and low-weight bulimia nervosa: case reports, Int. J. Eat. Disord. 44 (3) (2011) 269–275, https://doi.org/10.1002/eat.20807.
[116] C. Tufanaru, Z. Munn, E. Aromataris, J. Campbell, L. Hopp, Chapter 3: Systematic reviews of effectiveness, in: E. Aromataris, Z. Munn (Eds.), JBI Manual for Evidence Synthesis, JBI, 2020.
[117] J.L. Tully, A.D. Dahlén, C.J. Haggarty, H.B. Schiöth, S. Brooks, Ketamine treatment for refractory anxiety: a systematic review, Br. J. Clin. Pharmacol. 88 (10) (2022), https://doi.org/10.1111/bcp.15374.
[118] S. Ulfvebrand, A. Birgegård, C. Norring, L. Högdahl, Y. von Hausswolff-Juhlin, Psychiatric comorbidity in women and men with eating disorders results from a large clinical database, Psychiatry Res. 230 (2) (2015) 294–299, https://doi.org/10.1016/j.psychres.2015.09.008.
[119] B.T. Walsh, Phenelzine vs Placebo in 50 Patients With Bulimia, Arch. Gen. Psychiatry 45 (5) (1988) 471, https://doi.org/10.1001/archpsyc.1988.01800290091011.
[120] B.T. Walsh, A.S. Kaplan, E. Attia, M. Olmsted, M. Parides, J.C. Carter, K.M. Pike, M.J. Devlin, B. Woodside, C.A. Roberto, W. Rockert, Fluoxetine After Weight Restoration in Anorexia NervosaA Randomized Controlled Trial, JAMA 295 (22) (2006) 2605–2612, https://doi.org/10.1001/jama.295.22.2605.
[121] C.M. Webb, P. Thuras, C.B. Peterson, J. Lampert, D. Miller, S.J. Crow, Eating-related anxiety in individuals with eating disorders, Eat. Weight Disord. 16 (4) (2011) e236–e241, https://doi.org/10.1007/bf03327466.
[122] B.M. Williams, C.A. Levinson, A model of self-criticism as a transdiagnostic mechanism of eating disorder comorbidity: a review, N. Ideas Psychol. 66 (2022) 100949, https://doi.org/10.1016/j.newideapsych.2022.100949.
[123] P.E. Wolfson, J. Andries, D. Ahlers, M. Whippo, Ketamine-assisted psychotherapy in adolescents with multiple psychiatric diagnoses, Front. Psychiatry 14 (2023), https://doi.org/10.3389/fpsyt.2023.1141988.
[124] World Health Organization. (2022). *ICD-11: International classification of diseases (11th Revision)*. Icd.who.int. ⟨https://icd.who.int/browse/2024-01/mms/en#1412387537⟩.
[125] Z. Yilmaz, M. Halvorsen, J. Bryois, D. Yu, L.M. Thornton, S. Zerwas, N. Micali, R. Moessner, C.L. Burton, G. Zai, L. Erdman, M.J. Kas, P.D. Arnold, L.K. Davis, J. A. Knowles, G. Breen, J.M. Scharf, G. Nestadt, C.A. Mathews, C.M. Bulik, Examination of the shared genetic basis of anorexia nervosa and obsessive–compulsive disorder, Mol. Psychiatry 25 (9) (2018) 2036–2046, https://doi.org/10.1038/s41380-018-0115-4.