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Binge eating disorder

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Abstract

Binge eating disorder (BED) is characterized by regular binge-eating episodes during which affected individuals ingest comparably large amounts of food and experience loss of control over their eating behavior. The current worldwide prevalence of BED is estimated to be at least 1.3%. BED is commonly associated with obesity and with somatic and mental health comorbidities. People suffering from BED experience considerable burden and impairments in quality of life, at the same time, BED often goes undetected and untreated. The aetiology of BED is complex, including genetic and environmental factors as well as neuroendocrinological and neurobiological contributions. Neurobiological findings highlight impairments in the domains of reward processing, inhibitory control and emotion regulation in people affected by BED, and these neurobiological domains are currently targets for emerging treatment approaches. Psychotherapy is currently the first-line treatment for people with BED. Recognition and research on BED has increased since its inclusion into DSM-5, however, continuing efforts are needed to understand underlying mechanisms of BED and to improve prevention and treatment outcomes for this disorder. These efforts should also include screening, identification, and implementation of evidence-based interventions in routine clinical practice settings like primary care and mental health outpatient clinics.

[H1] Introduction

Binge-eating disorder (BED) is a newly introduced eating disorder diagnosis in DSM-5[1] and the ICD-11[2] (**Figure 1, Table 1 and Box 1**). The core psychopathology characterizing BED includes regular binge-eating episodes during which affected individuals ingest comparably large amounts of food in a discrete time period, e.g. within any 2-hour period, while experiencing loss of control over their eating behaviour[1]. In order to fulfill the full-syndrome diagnosis according to DSM-5[1], these episodes have to occur at least once a week for at least three months and have to be associated with distress regarding binge-eating (see Table 1). Moreover, binge-eating episodes are associated with at least three of the following five characteristics: eating (a) much more rapidly than normal, (b) until feeling uncomfortably full, (c) despite not feeling physically hungry, (d) alone because of embarrassment about the amount; and (e) negative feelings after overeating[1]. BED and the eating disorder bulimia nervosa (BN) are both characterized by regular binge-eating episodes[1], however, while the regular use of one or more inappropriate compensatory behaviours to prevent weight gain, such as self-induced vomiting or fasting, is part of the diagnostic criteria for BN[1], individuals affected by BED do not regularly compensate using inappropriate methods. Moreover, the diagnostic criteria for the eating disorders anorexia nervosa (AN)[3,4] and BN also incorporate disturbances associated with body image, such as overevaluation of weight and shape, whereas this is not required for a BED diagnosis[1].

Comparable to other mental disorder, the pathophysiology of BED is complex and multifactorial, with biological, individual and social variables contributing to dysregulated eating and other related behaviours seen in individuals suffering from BED. Recent neurobiological accounts on the aetiology and maintenance of BED propose that dysfunctions across the spectrum of impulsivity might lie at the core of BED, which include alterations related to reward processing, inhibitory control as well as emotion regulation.

BED constitutes an important health issue as it is a highly prevalent eating disorder in the general population[5-7], but commonly overlooked and is often associated with obesity and extreme obesity[7].

Up to 30% of individuals with obesity seeking behavioural or surgical weight loss treatment have co-occurring BED[8,9]. This highlights the clinical importance of this eating disorder, especially given that the World Health Organization has identified the worldwide obesity "epidemic" as one of the major global health problems[10], and average Body Mass Index (BMI) continues to rise globally[11]. However, regarding the considerable association between elevated BMI and BED, it should be noted that weight loss as a treatment outcome for BED is controversial, with current treatment guidelines prioritizing behavioral outcomes such as reduction in or abstinence from binge-eating as a primary treatment goal for BED[12,13].

This Primer on BED focuses on epidemiology, comorbidity, etiological and maintenance mechanisms of BED, as well as diagnosis and screening, prevention, and management approaches for BED and quality of life of affected individuals. The Primer predominantly focuses on current evidence on BED in adult populations. Due to the rapidly developing field, we are also outlining emerging fields of research, especially with respect to novel innovative treatment approaches. Given the frequent comorbidity of BED with obesity, the Primer outlines what is necessary to know about differential diagnosis and management of BED across the obesity spectrum; however, the Primer will not give a general overview on the evidence related to treatment of obesity as this has been covered previously[14].

[H1] Epidemiology

The epidemiology of BED is still emerging. Present understanding of the epidemiology of BED is based on clinical and community-based studies conducted in North America, Australia, and Europe. Information from other parts of the world is still preliminary. Estimates of occurrence of BED are highly disparate (Figure 2).

[H2] Prevalence and incidence

The incidence of BED ranges from 35 to 343 per 100 000 person-years, but these estimates are based on only two studies of young women.[15,16] The World Mental Health Survey[17] provided the first population-based estimates of the prevalence and correlates of BED among adults in different countries: estimates varied widely across settings. In a meta-analysis of studies completed before the year 2018, past-year prevalence of DSM-5 BED in adults was estimated to be 1.3% (95% CI 0.6-2.3%): 0.3% (95% CI 0.1–0.6%) for men and 1.5% (95% CI 1.2–1.7%) for women[5]. However, methodologically rigorous population-based studies of BED completed after the meta-analysis have arrived at widely varying estimates (0.2%-3.6% for women, 0.03%-1.2% for men) [18].

Highest past-year prevalences have been reported for adolescents (1.8–3.6% for girls, 1.5% for gender-diverse youth, and 0.2–1.2% for boys) [19,21]. Their symptoms may be transient: in a longitudinal community study, 6.1% of adolescent girls met DSM-5 diagnostic criteria for BED in at least one assessment, but only few met BED criteria over time[22].

A potential explanation for widely varying estimates of occurrence is a social constructivist view of psychiatric diagnoses. Psychiatric diagnoses try to "make meaning" out of information that is inherently ambiguous and dynamic and more likely to reflect the diagnostician's training and context than underlying biological mechanisms. For this reason, a careful study of local meanings and conditions is important. Critical researchers have also pointed out that the construct "BED" is deeply rooted in Western consumer culture[23]. For this reason, the global relevance of BED is still unclear.

[H2] Burden of disease, deaths and morbidity

BED is associated with a considerable burden of disease and excess mortality[24] [25]. Reports based on specialist clinics in Europe estimate that the standardized mortality ratio associated with BED is 1.50 (95% CI 0.87–2.40) [9] to 1.77 (95% CI 0.60-5.27) [8]. Yet, the healthcare needs of individuals with BED are rarely met. In high-income countries, <10–50% of individuals with BED receive care [15,26,27], perhaps

because addressing BED often requires highly specialized expertise. In a nationally representative study of US adults, past-year health conditions commonly co-occurring with BED included obesity, hypertension (31%), various heart conditions (17%), arthritis (24%), elevated cholesterol (27%) and triglycerides (15%), diabetes (14%), smoking (40%), sleep problems (29%) and general poor health [28,29].

[H2] Co-occurring conditions and mental health issues

Obesity and metabolic syndrome are common consequences of BED, and BED is particularly prevalent among individuals with Type 2 diabetes[30] and among bariatric surgery candidates[31]. In a nationally representative study of US adults, the mean body mass index of participants with BED was 33.9 kg/m^2[7]. BED often co-occurs with other mental health conditions. In a nationally representative study of US-based adults, 94% of individuals with BED met diagnostic criteria for at least one additional psychiatric disorder [28] and 23% of individuals with BED had attempted suicide [32]. Common comorbid conditions of BED include lifetime mood disorders (70%), posttraumatic stress disorder (32%), and anxiety disorders (16%) [28]. Disorders characterized by poor impulse control[33] are also frequent, including borderline personality disorder[28], alcohol disorder[28], and pathological gambling[34]. Attention-Deficit/Hyperactivity Disorder also co-exists with BED[35]. In particular, individuals with BED who seek obesity surgery report serious problems with impulse control before surgery, such as intermittent explosive disorder, gambling, and compulsive buying[36].

[H2] Sociodemographic factors

BED was included in the ICD-11 diagnostic system in 2018 (Box 1). For this reason, most research on BED has been conducted in the US, where BED is prevalent in all socioeconomic groups[37]. Issues with weight and weight-related teasing, body dissatisfaction, and dieting are key risk factors for binge-eating[38]**.** Overevaluation of weight and shape is associated with greater BED-related functional impairment[39]. However, people who have experienced poverty, violence, traumatic events, combat, food insecurity or major mental illness appear to be at an elevated risk for BED[40-45]. Several mostly US-based reports suggest that the prevalence of BED may be elevated in black and Latino populations [7,46-

[48] and among sexual minorities compared to the general population. [49-51] In US and Australia, recent immigrants were at a lower risk[52] and indigenous people[53] at an equal or higher risk for BED than the general population. Stigma and stereotypes associated with gender, mental health, weight, age and various disadvantaged positions, such as disability and lack of resources, may decrease the visibility of BED[54]. For this reason, prevention, detection and management of BED is a medical question, but at the same time is also a question of social justice.

[H1] Mechanisms/pathophysiology

The pathogenesis of BED is still widely unclear.

However, several studies in BED have described biological and neural mechanisms associated with BED symptomatology, suggesting that underlying alterations in biological and neural levels are linked to binge eating episodes[55].

[H2] Food intake regulation pathways

Different pathways regulating food intake might be related with overeating in BED **(Figures 3, 4)**. Hunger and satiety are regulated by the gastrointestinal, endocrine, and nervous system through the integration of signals at different levels (i.e., hormonal, neuronal and metabolic, behavioral and cognitive)[56]. At a neuroendocrine level, a central structure for homoeostatic control is the hypothalamus[57] **(Figure 3)**. Ghrelin is secreted from the gastrointestinal tract signalling lacking nutrients, and this increases motivation to seek food, whereas leptin works on hypothalamic peptides in the central nervous system enhancing satiety signals[57] **(Figures 3, 4)**. From hunger to satiety states, a cascade of endocrine satiety signals, in addition to ghrelin and leptin, support meal completion through the release of peptide hormones such as cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1), and peptide YY (PYY)[58,59] **(Figure 4).** Moreover, other neurotransmitters such as dopamine, endogenous opioids and endocannabinoids also modulate food intake by regulating rewarding aspects of foods (e.g., increasing orosensory or palatability of foods).

To date, there is a scarcity of studies on neuroendocrinological alterations in BED as well as in other forms of overeating such as grazing. However, in populations suffering from loss of control eating, which is also a characteristic of BED, dysregulated peptide hormone functioning has been reported, including lower levels of fasting ghrelin and higher levels of leptin, dysregulated post-meal ghrelin concentrations as well as alterations regarding CCK, and peptide YY[60]. Such alterations could suggest a resistance to satiety signalling in individuals suffering from binge eating that can be a risk factor to trigger uncontrolled food intake.

[H2] Underlying brain regions

From a neurobiological perspective, the hypothalamus is critical in homeostasis modulating peripheral metabolic signals and the motivational circuits, as it also receives afferent dopaminergic transmission from the nucleus accumbens (NAcc), the core area of the reward system in the striatal regions. Corticostriatal circuits are connected to regulate motivated behaviour in response to reward stimuli such as food or money. It has been hypothesized that alterations in corticostriatal circuits are due to the excess consumption of high-calorie and palatable food[61]. The increased activity in striatal regions is associated with dopaminergic signalling promoting craving for food, similar to craving in individuals with substance use disorder. In patients with BED, neuroanatomic and neurofunctional alterations in corticostriatal circuits have been the most consistent finding associated with the severity of eating disorder symptomatology[55]. Since the corticostriatal circuit has a regulatory role on motivation and impulse control, problems in the inhibitory control described in BED can be implicated in increased binge eating behavior[61].

It has been observed that individuals with BED exhibit distinctive neural activation patterns during tasks involving inhibitory control and reward processing **(Figure 5)**, as compared to people with obesity and without a BED[62-64]. Decreased inhibitory control has been associated with diminished activity in the vmPFC, inferior frontal gyrus (IFG), and the insula in individuals with BED as compared to the general population[65].. During a fMRI Stroop color-word interference task, individuals with BED displayed a more diminished activity in the vmPFC, inferior frontal gyrus (IFG), and the insula than individuals with obesity or healthy controls[65]. It has been suggested that structural and functional changes in brain regions involving frontal and striatal networks[66], including those involved in emotional processing[55], may be associated with uncontrolled eating in patients with BED. These corticostriatal circuitry alterations could be contributing to overeating, often acting as a way for short-term alleviation of negative emotions[67]. Putative relationships between emotion processing and binge eating which are mirrored in these neurobiological findings have been proposed by the emotion regulation model[67] as well as the interpersonal model of BED[71]. The emotion regulation model outlines

the role of negative affect as trigger for binge eating[67], while the interpersonal model suggests that interpersonal problems might be a significant source of negative affect in BED[71].

[H2] Cognitive impairments in BED

Systematic reviews have reported cognitive impairments in BED when assessed with neuropsychological tasks[72]. Regarding specific domains, individuals affected by BED showed lower performance in decision-making, inhibitory control and cognitive flexibility as well as an attenuated food-related attentional bias, when compared with healthy participants[68,72-74]. This poor performance has been also described in individuals with substance usedisorders, behavioural addictions or BN, suggesting a similar impairment in prefrontal executive function[70,75]. The cognitive impairment in BED was associated with higher BMI[76], although higher impulsivity was also reported for individuals with normal-weight affected by BED[77]. Moreover, cognitive impairment was associated with higher ED severity, and greater general psychopathology[76] and with poorer therapy outcomes[78]. In general terms, some of these cognitive impairments seem to be remediable[79]. However, some studies found a greater relevance of comorbid psychopathology in individuals with BED, namely depressive symptomatology, than cognitive dysfunction for therapy outcomes[80].

Decision-making is a complex cognitive process, involving conscious and habitual components, which ultimately results in the choice of an outcome over other alternatives. There are different decision-making circumstances, for instance, requiring choices under conditions of ambiguity. Patients with BED have been shown to take riskier decisions in tasks involving decision-making under ambiguity as compared to obese individuals without BED and as compared to normal-weight individuals[81]. Another facet of decision-making refers to delay discounting which comprises the ability to resist an immediate smaller reward in favour of a later larger incentive. Previous research has found high delay discounting rates to be associated with overeating and its reward value, namely in BED and obesity[82-85], but also with specific personality traits including impulsivity[85,86], among other psychiatric disorders[82]. Lack of delayed reward was associated with specific neural circuitry associated with limbic system and

hypoactivation of inhibitory control, mediated by PFC, namely dmPFC[87]. Choosing immediate rewards over delayed rewards, based on emotional states, has been found to be more common in BED than in healthy controls or disorders characterised by high levels of dietary restriction, such as AN[85]. Hypoactivation in the anterior insula may underlie increased delay discounting in individuals with BED[87].

[H2] Genetics

BED aggregates in families [88,89] and this is independent of obesity[89]. Twin and family studies of BED, using varyingly broad definitions of illness, have estimated its heritability to be between 0.39 and 0.57 (Ref[90-92]). The study of molecular genetics of BED has lagged behind that of other eating disorders, particularly AN. Although the field of psychiatric genetics has progressed beyond candidate gene studies, we acknowledge two reviews of historical interest. One reviewed all candidate gene studies in the literature and identified several investigated polymorphisms that had weak evidence of association in BED largely due to small sample size (many <100 cases or controls) and variable replication (i.e., 5-HTTLPR (5-HTT), Taq1A (ANKK1/DRD2), A118G (OPRM1), C957T (DRD2), rs2283265 (DRD2), Val158Met (COMT), rs6198 (GR), Val103Ile melanocortin receptor gene (MC4R), Ile251Leu (MC4R), rs6265 (BDNF), and Leu72Met (GHRL)[93]. *MC4R* is of particular interest due to its known roles in energy homeostasis, food intake, satiety, and body weight[94]. A systematic review and meta-analysis of six studies evaluated the association between coding variants in the MC4R gene and BED in individuals with obesity [95]. The analysis yielded a significant positive association between gain-of-function (GOF) variants in the MC4R and BED (odds ratio [OR] = 3.05; 95% confidence interval [CI]: 1.82, 5.04; $p = 1.7 \times 10^{-5}$), with no significant association observed with loss-of-function (LOF) mutations (OR = 1.50; 95% CI: 0.73, 2.96; p = 0.25). Adjusting for study quality did not appreciably alter results. However, the included studies were judged to be of low quality and have serious risk of bias, limiting confidence and generalizability of the results.

In the absence of GWAS, one study has used polygenic risk scoring (PRS) to explore differences across eating disorders (AN, BN, and BED) in the UK Biobank [96]. In terms of psychiatric traits and disorders, BED was positively associated with PRS for schizophrenia, major depressive disorder, and attention-deficit hyperactivity disorder (ADHD). BED showed positive associations with several anthropometric traits including waist circumference, hip circumference, overweight, obesity, extreme BMI, and childhood obesity —the opposite pattern as seen in anorexia nervosa. BED was negatively associated with the age at menarche PRS, meaning that increased genetic risk for BED was associated with increased genetic risk for earlier age at menarche. Notably, whereas the associations with PRS for psychiatric traits were similar across eating disorders (with the exception of ADHD only being associated with BED), the associations for anthropometric traits diverged considerably between AN and BED[96]. Associations between BED and PRS for overweight and obesity were replicated in a second sample. This study was the first to show similarities across eating disorders in genomic psychiatric liability, but divergent underlying biology in body mass regulation. Large GWAS are needed in order to confirm these observations.

[H2] Intestinal Microbiota

The intestinal microbiota comprises trillions of microorganisms that inhabit the gastrointestinal tract, including bacteria, virus, archaea, eukaryotes, and fungi. Emergent research points to a role of the intestinal microbiota in both physical and psychological wellbeing[97]. The intestinal microbiome represents the cumulative genomes of the intestinal microbiota and contributes to important functions such as digestion and absorption of calories from the gut[98]. The gut microbiome can be influenced by short- and long-term dietary changes[99,100] and has been associated with adiposity [101] and various mental disorders via the gut-brain axis[102], including AN[103]. Several hypotheses have been forwarded regarding the potential role of the intestinal microbiota in BED[104] including a dysbiosis or particular microbial composition that may influence host food choice[105], the impact of short chain fatty acids (SFCA) produced by intestinal bacteria on dysregulated appetite[106], and the impact of the gut-brain axis on mood with binge-eating serving as an emotion regulation strategy[107-109].

One small empirical investigation has explored the composition of the gut microbiota from stool samples of 42 individuals with obesity and BED in comparison to 59 individuals with obesity and no BED using 16S rDNA sequencing[110]. Individuals with BED displayed increased levels of *Anaerostipes* and decreased *Akkermansia*, *Desulfovibrio,* and *Intestinimonas*. Although one could conjecture the meaning of these bacterial shifts based on known effects of the genera that differed significantly, replication in larger well-characterized samples is recommended before definitive interpretations or causal conclusions can be drawn. Moreover, this study only included individuals with obesity, and says nothing about the intestinal microbiota in individuals who have BED, but do not have overweight or obesity. The study of the intestinal microbiota and intestinal microbiome in BED is in its infancy and no recommendations can be made regarding novel treatments that target the intestinal microbiota, until larger scale, standardized, and well-controlled studies are completed.

[H1] Diagnosis, screening and prevention

As BED is a fairly new diagnosis in official diagnosis systems of the western world (DSM-5, ICD-11), variability across countries is not well examined[6]. For example, BED has not been included in the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) 2019, though globally, it has a high prevalence rate and causes significant burden [24]. In western countries, health care professionals and the public are often not aware that BED is a discrete eating disorder [111]. Related to this research-practice-gap, the dissemination of screening, prevention and management for BED seems low established across the globe [112,113].

DSM-5 classifies BED as an eating disorder characterized by recurrent episodes of binge-eating accompanied by feelings of loss of control[1]. The term binge-eating entails the ingestion of an unusually large amount of food in a discrete period of time. Studies that have attempted to quantify the amount ingested during such a binge-eating episode report quantities between 3000-4500 kcal[114]. The DSM-5 defines five criteria for BED **(Table 1)** which have to be fulfilled in order to assign the diagnosis. Moreover, the binge-eating episodes have to accompanied by at least three out of five common

characteristics[1]. ICD-11 classification of BED is broadly in accordance with DSM-5 (Box 1), except for the time criterion regarding frequency of binge-eating and size of binge-eating episode, which are more liberal in ICD[2]. As Figure 1 outlines, there has been some change especially regarding the time criterion during the process of recognizing BED as an official diagnosis, impacting prevalence estimates and transition between eating disorder diagnoses[115]. In the DSM-5, binge-eating frequency is used to determine the severity of BED[1], with one to three episodes per week being classified as mild, four to seven as moderate, eight to thirteen as severe, and with fourteen or more episodes per week classifying as extremely severe. The severity may be assessed higher if other symptoms and the degree of functional impairment are additionally considered. First studies conclude that this DSM-5 severity specifier is valid[116], whereas others propose to specify BED severity according to overvaluation of shape and weight[117].

Partial remission from BED is fulfilled if, after full criteria were previously met, binge-eating frequency is reduced to less than once per week for a sustained period of time[1]. DSM-5 does not specify the duration of this sustained period of time. If none of the DSM-5 criteria for BED which were previously met have been fulfilled for a sustained period of time, a person is in full remission according to DSM-5[1]. ICD-11 does not determine severity or partial remission of BED[2].

Regarding help-seeking behaviour, data from the US suggests that only about 50% of affected persons with BED are ever seeking help for their eating disorder, with lower help-seeking rates in men and in ethnic minority groups [27]. The most frequent barriers to help-seeking behaviour experienced by affected patients are stigma and shame[118]. People affected by BED often seek for help with the aim to lose weight and are sometimes even not aware that they have an eating disorder[113] as public awareness concerning BED is still low [111]. Children and adolescents often do not meet full criteria for BED, but show “loss of control eating”, a concept in which the amount of food eaten is considered less relevant, as children often have restricted access to food or increased difficulties to quantify the amount eaten[119].

[H2] Screening tools and assessment

As eating disorders, and BED in particular, are common mental disorders, yet are often unrecognized and undertreated[120], effective screening tools and diagnostic strategies are essential. Due to the considerable overlap between obesity and BED[7] and a higher prevalence of BED in populations seeking out treatment for weight loss[8,9], screening for BED is especially important in these risk groups. The most commonly used screening tool for eating disorders in the general population is the 5-item SCOFF (*S*ick, *C*ontrol, *O*ne, *F*at and *F*ood) questionnaire[121]. However, BED had not yet been defined at the time when the SCOFF was developed. In the meantime, a series of specific self-report instruments and expert interviews have been developed, which also capture the diagnostic criteria of BED based on DSM-5 **(Table 2)**. Structured clinical expert interviews are considered as gold standard for the diagnosis of BED[12] **(Table 2)**. For patient groups at high risk for BED, such as patients with obesity assigned to receive surgery for weight loss, general recommendations have been published towards a combination of an established self-report instrument (e.g., EDE-Q) with an expert interview (EDE)[122].

Generally, single measures, for instance such as BMI or a screening score, should not be used as a sole basis to decide whether a person should be offered treatment[12]. Across health care settings, clinicians should routinely conduct confidential psychosocial assessments that include questions regarding eating behaviour, body image, and mood in patients at risk for an eating disorder[123]. In addition, they should monitor patients' weight and height in terms of BMI including the respective percentiles changes and growth curves for children and adolescents to identify the favorable window for early intervention. Besides considering BMI, diagnostic assessment for a potential BED should explore weight history including weight cycling and extreme body weight, eating patterns including irregular, restrictive and selective eating as well as overeating and feelings of loss of control, compensatory and exercise behaviours as well as body image including dissatisfaction and preoccupation with weight and shape[123].

As other eating disorders and as obesity, BED is associated with considerable stigma[54] and shame[124]. Both can result in fear and reticence towards help seeking and disclosing eating disorder symptoms[54] and especially experienced stigma or frank discrimination has been identified as contributing to symptoms of distress and depression as well as a maintaining maladaptive eating behaviour[54]. A nonjudgmental and motivational stance has proven successful in establishing a working alliance with patients affected by eating and weight disorders[123].

[H2] Medical morbidity and complications in BED

Because of the high prevalence of BED, especially in those with marked obesity, the parameters of a metabolic syndrome[125,14] should be systematically assessed, in this subgroup. Based on the harmonized definitions and clinical criteria, waist circumference, triglycerides, low density lipoprotein cholesterol and fasting blood glucose should be recorded in addition to anthropometric parameters (weight and height), weight history, and blood pressure[14]. In particular, as diabetes is a major concern for patients with BED, a stepwise evaluation of blood glucose levels is encouraged.

Studies of individuals with BED demonstrated elevated metabolic as well as inflammatory markers associated with increased morbidity and mortality[126]. Up to 20% of patients with type 2 diabetes (T2DM) have an underlying, yet often undetected, eating disorder, the most common of which is BED [127]. This is especially relevant as binge-eating behaviours have been shown to worsen metabolic markers, including glycemic control[127]. Type 1 diabetes (T1D) as well as other autoimmune associated disorders were also more common in individuals with BED than referent controls[128]. In two pilot studies, 23%[129] to 28%[130] of people with nonalcoholic fatty liver disease (NAFLD) screened positive for BED, with this pattern of comorbidity probably arising from shared risk factors including obesity, insulin resistance, metabolic syndrome, and an unfavourable body composition[130].

Individuals with BED in the general population report a range of gastrointestinal (GI) symptoms, including dysphagia, acid reflux, bloating, abdominal pain, diarrhea, constipation, and lower GI urgency[131]. BED appears to be associated with both upper and lower GI symptoms, independent of

411 the level of obesity[131]. Additionally, respiratory (30%) and musculoskeletal problems (21%) are
412 significantly increased in patients with BED compared with the general population[132]. Wassenaar et
413 al.[126] highlighted that patients with BED—particularly due to obesity and increased risk for T2D—have
414 multiple risk factors for cancer, including colorectal cancer, esophageal adenocarcinoma, pancreas
415 and liver cancer, as well as cancer of the gallbladder, kidney, postmenopausal breast, endometrial,
416 thyroid, ovarian, and prostate cancer. Another important field of health concerns in the BED
417 population includes urinary incontinence as well as polycystic ovarian syndrome (PCOS), which is again
418 associated with insulin resistance and increased risk of infertility[133]. Between 17 and 23 % of patients
419 with PCOS meet criteria of BED[133].

420 ***[H2] Differential diagnosis***

421 Regarding the core criterion of BED which is binge-eating, it is important to recognize that a
422 considerable subgroup of patients shows overlap with other patterns of maladaptive eating and
423 overeating, for instance such as grazing which is defined as the uncontrolled intake of smaller food
424 amounts over prolonged time. *BED should be differentiated from grazing that is highly prevalent in*
425 *patients with BED, but not a diagnostic criterion, and also common in obese patients without BED and*
426 *patients with other eating disorders[134].* In addition to the differential diagnostic assessment from other
427 eating disorders (see introduction and Table 1), BED must be differentiated from other mental
428 disorders that may be associated with an increase in food intake. These include a subset of patients
429 with primary depressive disorder or bipolar disorder. BED should also be differentiated from
430 personality disorders, in particular borderline personality disorder, which can be associated with
431 impulsive behaviour, including binge-eating. Differential diagnosis should also exclude alcohol or
432 cannabis abuse or the use of other appetite-enhancing substances. In unclear cases, one must also
433 consider endocrine disorders (Cushing's syndrome, hypothyroidism, insulinomas), neurological
434 disorders (neuronal lesions to the medial hypothalamus, craniopharyngeoma) and rare genetic
435 syndromes (e.g. Prader Willi syndrome) as somatic differential diagnoses.

436 *Mental comorbidity in BED*

437 BED often co-occurs with other common mental disorders. Lifetime comorbidity with common other
438 mental disorders reaches over 90% in the general population[28] and in a study with a sample of > 600
439 treatment-seeking patients with BED, 41% had been diagnosed with a concurrent comorbid axis I
440 disorder, most commonly anxiety and mood disorders[135]. As it is the case with other mental disorders,
441 the temporal order of the emergence of comorbid conditions is often difficult to disentangle and they
442 might even dynamically evolve together as, in the case of BED, for instance there is considerable
443 neurobiological overlap in the regulation of mood and food intake. Psychiatric comorbidity was
444 associated with more severe BED pathology; however, it did not moderate weight loss, but patients
445 with comorbid mood disorders were less likely to remit[135] and therefore might be in need for different
446 or additional treatments. Depending on the complexity of the comorbidity pattern, the primary
447 condition should be clarified and treatments prescribed accordingly.

448

Natural course of BED

The evidence on the natural course of BED is heterogeneous, and again, mainly draws back on data from high-income countries. However, most long-term studies suggest that the natural course of BED is often long-standing, particularly in adult populations[18], with an average duration of 14-16 years [7,136]. Additionally, there is a high rate of transmission from a BED diagnosis to other eating disorders, in particular to Bulimia nervosa[7] and vice versa.

[H2] Prevention

Prevention efforts towards the establishment or maintenance of healthy eating behaviour and healthy body weight can be divided into measures and programs involving educational and behavioural interventions targeting the individual, and larger-scale interventions targeting structural and situational factors at the societal level.

Large-scale interventions are especially relevant in terms of the food environment which has been termed as being "toxic"[137] in most parts of the western world, i.e. an environment that encourages the consumption of high-fat, high-sugar food[137].. As such, there is considerable overlap between approaches to preventing obesity and eating disorders, including BED. In line with this, recent approaches have advocated universal prevention of eating and weight disorders[138]. It seems most likely that multi-component strategies integrating regulation of eating behavior and body weight might be most effective[14]. However, especially the effects of larger-scale efforts that incorporate policy-changes are often hard to conduct, making it difficult to identify which components are effective[139]. Further, these system-level approaches mostly do not have the explicit goal of preventing binge eating or BED and there is scant evidence if they are helpful in doing so. Individuals at risk for binge eating might profit from prevention efforts on a societal level, which predominantly address factors contributing to food choices and opportunities to be physically active in an individual's everyday life[140]. Potential leverage factors include for instance the frequency of family meals, quality of food and access to unhealthy food at workplace or school cafeterias, availability of supermarkets,

convenience stores, and fast-food restaurants in the neighbourhood, industrial food marketing strategies, and governmental tax policy[141]. For example, one meta-analysis concludes that specific school policies concerning food and beverage availability can improve dietary behaviors[142].

Prevention strategies targeting the individual incorporate interventions derived from individual risk factor research. Retrospective data indicate that the first occurrence of BED is typically preceded by a series of stressful life events that may represent triggering factors, including for instance critical comments about shape, weight, or eating; or physical abuse[143]. However, very similar life events were also found in a control group of women who developed a different mental disorder[143], underlining the challenges of targeted disorder-specific prevention efforts. Typical prospective antecedents of a BED diagnosis in girls comprised binge-eating, compensatory behaviours, weight/shape overvaluation, fear of weight gain, and feeling fat[144]. These prodromal risk factors predicted onset of BED with an accuracy between 67 and 83%[144], representing promising starting points for prevention efforts. On an even more fine-grained level, negative mood has been documented as an antecedent factor for the immediate triggering of binge-eating in BED[67], representing a highly relevant mechanism for both, prevention and management approaches. A meta-analysis documents that structured prevention programs using different approaches offered at universities to the high-risk population of students are effective in reducing the onset of sub-threshold or threshold eating disorders, predominantly by influencing dieting behaviour, drive for thinness and body dissatisfaction[145]. Another meta-analysis reveals that structured programs increasing media literacy are effective in reducing eating disorder risk in adolescents [146]. Looking at more targeted prevention efforts, cognitive dissonance approaches were most effective in reducing eating disorder risk factors[146] as well as future onset of eating disorders[147], and multi-component interventions proved to have stronger effects[146]. However, this targeted prevention approach has strongest effects in reduction of thin-ideal internalization[146], which is not the only risk factor or prodromal symptom for an emerging BED[144], and as most trials assess eating disorder symptoms as outcomes[146], it remains unclear if prevention efforts eventually translate into reduced diagnoses and if they are more useful to reduce one diagnosis over the other.

[H1] Management

[H2] Goals

Goals of treatment for BED include reduction or cessation of binge eating and associated psychopathology, improvements in mood and other psychiatric symptoms, improvement in metabolic indicators, such as HBA1c and finally also in quality of life. As outlined above, weight-related treatment targets such as stabilisation or reduction in weight are seen as controversial for BED. Evidence-based treatments for BED, recommended by international guidelines[12,148,149] include psychological therapies (particularly cognitive behaviour therapy (CBT)) and pharmacotherapy with second generation antidepressants, anti-convulsants (topiramate, zonisamide), CNS stimulants (lisdexamfetamine) and anti-obesity medications (orlistat). A network meta-analysis assessed comparative effectiveness of different BED treatments, including a total of 28 treatment comparisons, only one of which was pharmacological (2nd generation antidepressants vs lisdexamfetamine)[150]. Lisdexamfetamine is the only medication approved by the Federal Drug Administration (FDA) in the US for the treatment of BED, and only the second medication approved for the treatment of any eating disorder. Three contrasting outcomes were found: lisdexamfetamine was better at increasing binge abstinence than second generation antidepressants, therapist led CBT was better at reducing binge frequency than behavioural weight loss, but behavioural weight loss was better at reducing weight. Most other treatment comparisons revealed few between group differences[150].

[H2] Psychological treatments

International guidelines recommend an evidence-based psychological therapy is the first-line of care for a person with BED and for a considerable subgroup is sufficient treatment to achieve remission from binge-eating[12,148,149]. This is most usually in an outpatient setting but may be part of partial or full hospital programs with outpatient follow-up[151]. There are three main therapies with evidence of efficacy from randomised controlled trials, namely cognitive behaviour therapy[152] (CBT), interpersonal psychotherapy[153] (IPT) and dialectical behaviour therapy[154] (DBT). All are manualized[152-154] and have

been tested in group as well as individual formats. Table 3 summarises their key features. CBT has the most extensive evidence and adaptations to scalable forms such as guided and pure self-help[155], again with good outcomes in these less intensive deliveries from primary care health professionals. DBT has also a guided self-help form[156]. A network meta-analysis of 81 studies (7515 participants) identified 43 psychological therapy conditions (36 CBT) in an active arm and 14 of a structured self-help (7 guided and 5 pure self-help CBT) approach across the included studies[157]. Most trials of psychological therapies employed a wait-list control arm, female (90%) participants, with study mean ages in the mid-40 years, and a high (above 35 kg/m^2) mean BMI. The mean duration of BED was 17.9 years, and mean number of therapy sessions was 16.5 weeks. In this review[157], there were moderate effect sizes at end of therapy for reduction of binge-eating, other eating disorder psychopathology and improved mood for full and guided therapies, and significantly greater improvements comparted to wait list, but not in regard to BMI. Similar findings were reported for self-help interventions[157]. Improvements were generally maintained at 6 and 12 month follow-ups. Unusually there was a small but significant increase in lost-to-follow-up assessments in the active psychotherapy condition compared with wait list control condition. Quality grades were also low to very low, mostly due to limitations in study design or execution (risk of bias), inconsistency (e.g., high heterogeneity), lack of direct evidence, and imprecision (low confidence). IPT is an evidence-based treatment for BED and has proven effective in RCTs when compared to behavioural weight loss treatment, guided self-help[158] or CBT[159]. A recent meta-analysis on the efficacy on DBT in BED summarizes that this evidence-based treatment form demonstrated greater efficacy compared with the control group in improving emotion dysregulation and eating disorder psychopathology[160]. Few 'head to head' comparisons of psychological therapies have been reported[157]. In three trials, CBT reduced binge-eating days more than a humanistic therapy, IPT or focal psychodynamic therapy but no other significant differences were observed. However, CBT resulted in greater improvements in binge-eating and other eating disorder symptoms than DBT in an RCT[161]. Psychological therapy outcomes did not differ from those of combination psychological and pharmacological therapy, but attrition was lower with psychological therapy alone[157]. Overall, it

should be considered that whilst the majority of evidence is for CBT, overall the risk of bias is high across all psychological therapy trials due to lack of blinding and the use of inactive wait list control groups. Psychological treatments for BED can be often combined with treatments for comorbid conditions such as major depression. In addition, management of some comorbidities may be integrated into the BED therapy. In particular, mood intolerance/emotion regulation skills are an integral part of enhanced cognitive behaviour therapy (CBT-E)[152] and DBT[154]. Likewise, interpersonal deficits are integral to IPT[153] and to a lesser degree in DBT[154] and CBT-E[152]. Regarding moderators and predictors of treatment outcome in BED; there is a need for a specific synthesis in this area and findings have been hard to replicate, however, features associated with a better outcome are an early response to therapy (reduction of binge-eating within the first weeks), an absence of substance use disorder, lower age and BMI, and good premorbid interpersonal functioning[157,162], and recent data from CBT trials identified low weight concern as a predictor for remission[163] and a history of trauma as negative predictor of treatment success[164].. Overall, around half of people with BED achieve abstinence from binge-eating, which is maintained at 12-month follow-up; however, longer-term outcomes are less clear[165].

[H2] Pharmacological therapies

Box 2 provides an overview on drugs that have been tested in the treatment for BED in at least one RCT. Meta-analytic reviews[157,166] found that a range of pharmacological treatments of BED, mostly consisting of second generation antidepressants or the CNS stimulant lisdexamfetamine (LDX), have significant short-term effects on reducing or stopping binge-eating episodes compared with placebo, with inconsistent effects on eating disorder psychopathology and mood. However, most studies lack longer-term follow-up data. Available data on second generation antidepressants suggest that reductions in binge symptoms are no longer significant at 3-6 months follow-up[165]. One systematic review focused on combinations of psychological or weight loss therapies with medication, with the idea that these might be more 'potent' or helpful for patients with comorbidities[167]. However, only in two of 12 included trials (both with antiseizure medications) pharmacotherapy significantly enhanced

both binge-eating and weight outcomes, and only two (both with the weight-loss medication orlistat) modestly enhanced weight loss, but not binge-eating outcomes[167]. Lisdexamfetamine, a prodrug of d-amfetamine, is currently the only medication approved by the US Food and Drug Administration (FDA) for the treatment of moderate to severe BED in adults[168]. In short-term trials, LDX significantly reduces binge-days/week, improves associated psychopathology and reduces body weight by about 5-6%, with beneficial effects being seen from week one. In an open label 52-week extension of the short term trials,344 of 604 participants (57%) took LDX for the full 12 months extension[169]. In treatment completers, weight loss at 12 months was ~ 7.7 kgs. Common side effects in the short and longer term included dry mouth, headaches, and insomnia. Overall, the authors concluded that the safety and tolerability profile of LDX in adults with BED was broadly consistent with that in attention-deficit/hyperactivity disorder. One other study started with a 12-week, open-label phase during which the dose of LDX was optimised[170]. Of the 418 participants enrolled in the open-label phase of the study, 275 were deemed to be responders and were randomised to receive either LDX or placebo for a further 26 weeks. The proportions of participants meeting relapse criteria during the study period were 3.7% (5 of 136) for LDX and 32.1% (42 of 131) for placebo. Patients randomised to LDX had a significantly longer time-to-relapse (primary outcome) than those on placebo. The treatment-emergent adverse events observed were generally consistent with the known profile of LDX[170]. Two placebo controlled double-blind trials have evaluated the efficacy and safety of dasotraline, a novel dopamine and norepinephrine reuptake inhibitor, in adults with BED[171,172]. One trial[172] used once-daily, flexible doses (4, 6, or 8 mg/d) of dasotraline or placebo over 12 weeks in 315 adults. Treatment with dasotraline was associated with a significantly greater reduction in binge-eating days. Discontinuation due to adverse events occurred in 11.3% of patients on dasotraline vs 2.5% on placebo. The second trial[171] examined two fixed dosages (4 and 6 mgs of dasotraline vs placebo in 491 adults with BED, again over 12 weeks. At week 12, treatment with dasotraline was associated with significant improvement in number of binge-eating days per week only on 6 mg/d dose vs placebo, but not on the 4 mg/d dose. In both studies the most common adverse events on dasotraline were

insomnia, dry mouth, headache, decreased appetite, nausea, and anxiety. Changes in blood pressure and pulse were minimal. Both studies assessed dasotraline treatment as safe and effective, however, the company has withdrawn the drug development application and will not pursue it further for the treatment of BED.

[H2] Managing high body weight

As many people with BED have a high BMI with associated physical and mental health morbidity[28] numerous treatment trials have reported weight loss outcomes, and weight loss treatments have been trialled extensively. Most have reported short term greater weight loss with behavioural weight loss treatment (BWL) than with psychological therapies such as CBT, but there is less improvement in binge-eating frequency[11,157]. BWL is a psychobehavioural therapy which was developed for weight loss. It has some similarities to CBT in approach e.g., monitoring eating behaviour, but is not derived from psychological theory and is delivered by health professionals without formal psychological training. Findings on the efficacy of psychological treatments in inducing weight loss in people with BED have been inconsistent[173]. In one longer term trial psychological therapies had similar weight loss and better eating disorder outcomes at 2 years follow-up[158] but this was not found in another trial that had a 6-year follow-up[174]. "Weight-neutral" approaches have also been advocated in people with eating disorders for whom dietary restriction may risk relapse of binge-eating and other symptoms, and there is some evidence for their positive psychological and physical health (including increasing activity levels) outcomes generally[175]. Notwithstanding the need for caution, people with BED who also are medically compromised by a high BMI may benefit from approaches that integrate weight loss management with eating disorder treatment. There have been a small number of trials which have examined BWL in sequence with CBT following the BWL, e.g., the SMART stepped care trial (that started with BWL, then moved to CBT with additional randomisation to weight-loss medication or placebo)[176] and one RCT of an attempt at an integrated psychological therapy of CBT-E and BWL for people with disorders of recurrent binge-eating (i.e., BED, BN and OSFED)[177]. However, there was no

evidence for a superiority of a certain intervention sequence or an integrated approach for weight-loss and most BED outcomes[176,177].

On the other hand, there are demonstrable benefits supporting the need for psychological therapy for people receiving weight loss treatment such as surgery[178]. Pre-operative BED does not contraindicate obesity surgery and, according to recent meta-analytic data, seems not to influence weight loss after surgery[179], however, the number of high-quality studies in this field is limited. Binge eating can still occur after surgery[178], i.e. with intake of high caloric and easily digestible food despite the highly restricted stomach capacities, and binge eating pathology can return to pre-surgery severity in the long-term[180]. The post-operative prevalence rate of BED has recently been quantified at 4% over studies[181].

As outlined above, psychological therapies for BED are effective in reducing binge eating, while weight loss is not an aim of psychological therapies and not necessarily expected. However, there are data showing that there is wide interindividual variability in terms weight loss or gain over BED treatment and where binge eating abstinence is achieved with the help of psychosocial therapies, people do lose weight[182,183]. However, deficits in metabolism due to chronic dieting and restriction can contribute to maintenance of higher weight status.

[H2] Emerging treatments

A broad range of novel approaches to treating BED are being tested, some as stand-alone interventions others augmenting established treatments. Neurobiologically-informed multi-component psychological therapies, targeting impulsivity, inhibitory control and/or emotion regulation have been trialed with some success[184,185], however whether they are superior to more conventional cognitive behavioural treatments for BED is not clear. Neurocognitive approaches, including face-to-face cognitive remediation therapy (CRT) and various computerised trainings, focusing on processes related to inhibition, general and food-related impulsivity, and associated biases, have been used to reduce overeating and weight in BED and/or obesity[73,186,187]. CRT is a specific

653 psychotherapy approach which aims to improve neurocognitive functioning. A trial comparing CRT
654 with no treatment in 80 patients with obesity, of whom 70% reported binge eating, showed significant
655 improvements in cognitive flexibility, weight and binge-eating in the CRT group[188]. Feasibility trials of
656 different cognitive trainings, including attention, approach bias and inhibitory control training, have
657 been conducted with somewhat mixed results, given different methodologies, comparison groups and
658 training 'dose' [189-191]. Learning models suggest that exposure-based therapy may be effective in
659 reducing food cue reactivity, overeating, and body dissatisfaction in BED. In line with this thinking,
660 exposure interventions to illness-related stimuli (food, body) have been developed and tested in small
661 trials[192,193]. Increasingly, virtual reality (VR) enhanced approaches have been used to tackle food-
662 craving or food or body-related fears in bulimic EDs[194] with some success in reducing binge-eating. VR-
663 approaches rely on the creation and therapeutic use of computer-generated virtual environment
664 which exposes the person to stimuli that are closely related to disorder symptoms and foster the
665 opportunity for the person to develop and practice skills that reduce binge eating. An adjunctive VR-
666 CBT module added to a behavioural inpatient weight loss approach and focused on rescripting
667 negative body memories has been successful in supporting or maintaining longer term weight loss[195].
668 Beyond that, refinements of psychological treatment are developed and tested, for instance,
669 integrated cognitive-affective therapy (ICAT) which has an increased focus on affect intensity and
670 emotion regulation and might helpf patients with increased difficulties in these areas[196]. For
671 individuals with partners, a cognitive-behavioural couple intervention (Uniting Couples in the
672 Treatment of Eating Disorders-UNITE) have shown preliminary evidence of efficacy in the treatment
673 of BED[197]. Medications used in the treatment of type 2 diabetes, namely glucagon-like peptide-1 (GLP-
674 1) agonists, such as liraglutide and dulaglutide, are known to have both a peripheral and central effect
675 on appetite control. These medications have shown promise in reducing binge-eating and body weight
676 in patients with obesity[198] and in those with BED and diabetes[199].

677 Improved understanding of the neurocircuitry involved in EDs has given rise to the exploration of a
678 range of non-invasive neuromodulation (NIBS) treatments, such as repetitive transcranial current

679 stimulation (rTMS), transcranial direct current stimulation (tDCS), and neurofeedback[200,201]. A handful
680 of proof-of-concept or feasibility trials have used NIBS in populations with BED, a mixture of BED and
681 BN or obesity per se[202,166]. The potential of these interventions for the treatment of BED is as yet
682 uncertain. Combinations of neuromodulation interventions with different cognitive trainings are also
683 being piloted in BED[203,204]. It is as yet uncertain whether there are any synergistic effects.

684 **[H1] Quality of life**

685 In the context of health, quality of life (QoL) relates closely to the World Health Organization's (WHO)
686 conceptualisation of a person's subjective appraisal of their life across domains of environmental,
687 social, mental, and physical health status as may be measured by the WHO Brief QoL Assessment Scale
688 (WHOQOL-BREF)[205] and well-being with the WHO-5 Well-Being Index[206]. General measures of health
689 related QoL (HRQOL) (such as the WHOQOL-BREF and the Medical Outcomes Short Form (SF) health
690 survey 12 (SF-12)[207], inform the comparative level of health burden and cost utility estimates. A review
691 of HRQoL in eating disorders reported the most frequently used measure had been the SF-12 or its
692 parent version the SF-36[8]. Eating disorder illness specific instruments are also widely used e.g., the
693 Clinical Impairment Assessment scale[208]. Also, a measure of the family burden of caring for someone
694 with an eating disorder has been developed[209]. There is consistent and substantive evidence that
695 HRQoL is impaired in people with BED compared to people without an eating disorder in
696 representative community populations[8]. This impairment is commensurate with other eating
697 disorders. BED is associated with both physical and mental health morbidities such as high weight and
698 depression[8] (see Box 3). These observations apply both when the stricter DSM-5 definition of a binge
699 episode as objectively large or the broader ICD-11 definitions are applied[210]. It also translates into
700 personal and public health economic costs. A revision of the Global Burden on Disease estimates to
701 include BED found that of an 41·9 million estimated global eating disorders cases in 2019, 17·3 million
702 were people with BED, and they accounted for 0·8 disorders (95% UI 0·3–1·6) Disability Life Adjusted
703 years (DALYs)[24]. This was one fifth of the total DALYs due to eating disorders. Further research has

supported the impact of the presence of recurrent binge-eating, and the DSM-5 diagnostic specifier of distress related to binge-eating, on health state utility values (HSUVs; the 'Q' in Quality ALYs)[211]. Population estimates of fiscal costs for BED are high. In an Australian general population[212] study the total economic cost of an eating disorder was $84 billion from years of life lost due to disability and death, and annual lost earnings were $1.646 billion. These lost earnings peaked for both males and females aged 35 to 44 years, a period of high personal productivity. In this study, costs of BED were similar to those of other eating disorders, and binge-eating in itself accounted for 65% of the yearly financial cost of eating disorders. Health care use and costs are increased for people with BED. In a Swedish case register study[213] hospital and other health care costs were present for some years prior to and after their peak at the item of diagnosis and were also incurred for the treatment of comorbid problems. Under-treated or undetected BED is a major problem[214] that can increase personal, fiscal and health care burden. People with BED are likely to suffer additional effects from weight stigma, which diverts their treatment seeking to weight loss clinics and adds to treatment delays[214,215]. This adds to physical and psychiatric morbidity which has been found to be high in the general population and to comprise a large number of diverse disorders[28].

[H1] Outlook

Since its inclusion in DSM-5 in 2013[1], BED has received increasing recognition and the evidence base on this eating disorder is growing. The diagnostic criteria for BED have evolved over past decades (see Figure 1), and the relative novelty of this eating disorder diagnosis is also reflected in an ongoing nosological debate on how to best conceptualize BED. For instance, the concept of food addiction[216] has been introduced, a phenotype with large overlap with both, substance-use disorder as well as BED, assuming that especially ultraprocessed food can be "addictive" and trigger addictive-like eating patterns[216] including loss of control eating as it is seen within BED. Alternatively, impulsive eating patterns have been conceptualized as a behavioural addiction[217]. These different conceptualizations potentially have significant consequences for prevention and treatment approaches. At the same

time, there is little consensus regarding the introduction of such novel 'neighbourhood' diagnoses. Despite increased recognition and awareness and high prevalence estimates, research on many facets of BED lags behind the knowledge on the other two primary eating disorders diagnoses, AN and BN. These gaps in research cover important questions regarding epidemiology and quality of life, such as findings on the mortality of people with BED, which are more mixed and lower than for AN or BN[218]; and similarly, wider family and carer burden is also under-researched compared to these other eating disorders[218]. As can be seen in Figure 2, many areas of the world map appear 'white' meaning data lack on BED prevalence, and data estimating global burden of disease for BED have just been published[24]. Lacking data and awareness regarding epidemiology and burden of disease is problematic in many ways[219], not least, because eating disorder research in general is grossly underfunded in part due to the fact that the impact of eating disorders on the individual and society has often been neglected[24,219,220]. Genetics and epigenetics are other emerging fields in the study of BED, with currently very limited specific evidence. To date, no genome-wide association studies (GWAS) of BED have been conducted, although studies are in progress[221,222]. However, a strength of the field are advances in delineating the neurobiological mechanisms of BED which, together with more clinical findings[33], are supporting the view that individuals with BED represent a distinct phenotype within the obesity spectrum characterized by increased difficulties associated with reward processing, inhibitory control[73,74] and emotion regulation capacities[67]. This evolving basic research has led to translational research efforts, probing novel approaches which are informed by these mechanisms[185,187,189,200,201] and which can be important components in the management of BED. As in other field of mental health research, emerging novel methods from machine learning might contribute to a better understanding of disease mechanisms by integration of large-scale data as well as to a better prediction of the course and outcomes of BED[223].

Improving the outcome of BED treatment should be a main priority in the field in coming years—since the current first-line therapy achieves abstinence rates of 50%[165]. Within this endeavour, the common overlap between obesity and BED poses a major challenge: Both conditions share risk factors,

comorbidities and pathogenesis, yet, the optimal strategy remains unclear, both, for the field of prevention and management, e.g. if it is best to target weight loss and eating behaviour simultaneously, if it is best to choose one of these treatment goals and related interventions first or if one should pursue a "weight neutral" approach for patients with BED[175,176,224]. This applies in a very similar manner to another important priority which are prevention efforts: Currently, it remains widely unclear if successful BED and obesity prevention strategies are largely overlapping or how BED prevention would differ from obesity prevention, how we can guard against obesity prevention efforts promoting more binge-eating, and, regarding a more eating disorder focused perspective, how specific prevention approachs for BED would look like along the spectrum of different eating disorders.

An important next step, given that there is a considerable progress in the development of psychological treatments for BED, is to tackle the research-practice-gap and to ensure that evidence-based treatments are translated into clinical practice. Scalable solutions for the training of clinicians to deliver evidence-based psychotherapy have recently been proposed and investigated[225]. Another avenue for making evidence-based care more accessible for patients, not only during the COVID-19 pandemic, is the implementation of digital intervention and delivery technologies and strategies, also in terms of stepped-care-approaches[226].

Closely related to those important clinical questions is the notion that the large group of people affected by obesity is heterogeneous[14] with different phenotypes characterized by specific underlying vulnerability factors. Patients affected by BED represent one such phenotype—in order to be able to improve treatment outcomes for this patient groups, but also for other phenotypes, it seems important to implement assessment of eating behaviour, including binge-eating, into research studies investigating individuals on the overweight spectrum. A better characterization of study samples in terms of eating behaviour and eating disorders will help the field to learn more about individual vulnerability factors and to develop more targeted interventions. This approach will generally help advance etiological research on BED. This is vital as there is no current consensus model integrating

780 state-of-the-art evidence on different factors contributing to the etiology of this multi-factorial eating
781 disorder, although approaches looking at specific topics such as underlying neurobiological
782 mechanisms have been proposed[68]. It should be another priority for the coming years to work toward
783 and debate an integrated etiological model to encourage more theory-driven research in the field.
784 Ideally, such a model would go beyond the individual and also acknowledge the important influence
785 of environmental factors on the regulation of eating behaviour and body weight[141].

786 From a global health perspective, addressing the obesity epidemic, as it has been termed by the
787 WHO[10], constitutes one of the top long-term priorities for societies and health care systems
788 worldwide, and this is unlikely to be successful without a comprehensive consideration of eating
789 disorders, especially BED. In particular, the high impact of BED on individuals and society [24] (see Box
790 3), elevates the reduction of this burden to an additional long-term health priority.

791

Table 1. Diagnostic criteria (reduced version) of BED and differential eating disorder diagnoses according to DSM-5.

Criterion	BED	BN	AN
A	Recurrent episodes of binge eating. An episode of binge eating is characterized by both:[a] 1. Eating in a discrete period of time, an amount of food that is definitely larger than what most individuals would eat [a] 2. A sense of lack of control over eating [a]	Recurrent episodes of binge eating. An episode of binge eating is characterized by both: [a] 1. Eating in a discrete period of time, an amount of food that is definitely larger than what most individuals would eat [a] 2. A sense of lack of control over eating [a]	Restriction of energy intake relative to requirements, leading to a significantly low body weight [c]
B	Binge eating episodes are associated with three or more of the following: 1. eating much more rapidly 2. feeling uncomfortably full 3. not feeling physically hungry 4. alone because of feeling embarrassed 5.Feeling disgusted with oneself, depressed, or very guilty afterwards	Recurrent inappropriate compensatory behaviors to prevent weight gain, such as self-induced vomiting, misuse of laxatives, diuretics, or other medications, fasting, or excessive exercise. [c]	Intense fear of gaining weight or of becoming fat, or persistent behaviour that interferes with weight gain, even though at a significantly low weight.
C	Marked distress regarding binge eating is present.	The binge eating and inappropriate compensatory behaviors [c] both occur, on average, at least once a week for 3 months. [a]	Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation [b], or persistent lack of recognition of the seriousness of the current low body weight [c]
D	The binge eating occurs, on average, at least once a week for 3 months. [a]	Self-evaluation is unduly influenced by body shape and weight. [b]	NA
E	does not occur exclusively during the course of bulimia nervosa or anorexia nervosa	does not occur exclusively during episodes of anorexia nervosa	NA

AN: Anorexia Nervosa, BED: Binge Eating Disorder, BN: Bulimia Nervosa. Similarities between BED and BN/AN are marked with [a] , similarities between BN and AN with [b] and differences between BED and BN/AN with [c].

For AN, the DSM-5 defines two subtypes: (a) *Restricting type:* During the last three months, the individual has not engaged in recurrent episodes of binge eating or purging behaviour; weight loss is accomplished primarily through dieting, fasting

and/or excessive exercise. (b) *Binge-eating/purging type:* During the last three months the individual has engaged in recurrent episodes of binge eating [a] or purging behavior.

Data from Ref[1].

804 **Table 2.** Frequently used instruments to assess binge eating pathology (adapted from Parker &
805 Brennan, 2015[122]).

Instrument	Items	Description	Diagnostic instrument	References
Self-report instruments				
BEDS-7	7	Screening tool for BED assessing DSM-5 criteria	no	[227]
BES	16	Total score reflecting severity of binge eating behaviour	no	[228]
DEBQ	33	3 scales: Restrained eating, Emotional eating, External Eating	no	[229]
EDE-Q	28	Adapted from the EDE, global score & 4 subscales: Restraint, Eating Concern, Shape Concern, Weight Concern	no	[230]
EDI-3	91	12 scales: Drive for Thinness, Bulimia, Body Dissatisfaction, Low Self-Esteem, Personal Alienation, Interpersonal Insecurity, Interpersonal Alienation, Interoceptive Deficits, Emotional Dysregulation, Perfectionism, Asceticism, and Maturity Fears.	no	[231]
SDE		Screening tool for EDs in primary care	no	[232]
TFEQ	51	3 scales: Cognitive restraint, Disinhibition, Hunger	no	[233]
QEWP-5	28	Screening tool for BED assessing DSM-5 criteria	no	[234]
Expert Interviews				
EDE	40	current ED diagnoses, global score & 4 subscales: Restraint, Eating Concern, Shape Concern, Weight Concern	yes	[235]
SCID-5-RV	Module I	Feeding and Eating Disorders diagnoses according to DSM-5	yes	[236]

806 BEDS-7: 7-Item Binge-Eating Disorder Screener; BES: Binge Eating Scale; DEBQ: Dutch Eating Behaviour Questionnaire; ED:
807 Eating Disorder; EDE: Eating Disorder Examination; EDE-Q: Eating Disorder Examination Questionnaire, EDI Eating Disorder
808 Inventory; QEWP and QEWP-R: Questionnaire on Eating and Weight Patterns (Revised); SDE: Screen for Disordered Eating;
809 SCID-5-RV: Structured Clinical Interview for DSM-5 Disorders – Research Version; TFEQ: Three Factor Eating Questionnaire.

810

811 **Table 3** Manualised evidence-based psychological therapies for BED

Therapy	Theoretical model	Core elements
Cognitive Behavioural Therapy (CBT) Full, pure and guided self-help forms and CBT–enhanced (CBT-E)	CBT formulation - Core beliefs (overvaluation of shape and weight) initiate weight control behaviours that with negative mood states & life events initiate and maintain binge eating without compensatory behaviours.	Personalised psychoeducation Behaviour monitoring & experiments Cognitive restructuring & chain analyses Enhanced with modules for mood intolerance, clinical perfectionism, interpersonal deficits, low self-esteem
Interpersonal psychotherapy (IPT)	There is a bidirectional relationship between BED symptoms and interpersonal function mediated by self-esteem & negative affect. Focus on four problem areas (grief, role transitions, role disputes, interpersonal deficits).	Exploration of interpersonal function/current relationships (inventory) & for mulation Affect clarification & communication analysis A strong therapeutic relationship
Dialectical Behaviour Therapy (DBT) and and guided self-help DBT	Understanding the dialectic of opposing views of ED behaviours and their use in distress reduction.	'Meaning making' of symptoms as acceptance and change; Validation & Training in: mindfulness; distress tolerance; emotion regulation; & interpersonal effectiveness.

812

Figure legends

Figure 1: Timeline of the evolution of classification criteria for BED.

The first description of binge eating is attributed to the American psychiatrist Albert J Stunkard and dates to the late 1950s. These early notions focus on binge eating as a behaviour before it was recognized as a part of a disorder, and it took two decades until binge eating was introduced as a core symptom of a different eating disorders which is bulimia nervosa (BN) into the third edition of the DSM. Fourteen years later, BED was included as a research diagnosis into the fourth edition of the DSM, including a more specified definition of binge eating as a core psychopathology as well as a time criterion. It took another decade until BED was finally recognized as an official diagnosis in DSM-5. As compared to the research criteria, the DSM-5 criteria include a loosening of the time criterion with binge eating episodes at least once a week over three months necessary in order to fulfil the diagnosis. BED will also be incorporated into ICD-11, and the ICD has loosened criteria around the 'large amount' of food ingested, allowing subjective binge eating, which will put challenges towards consistent application of diagnostic criteria.

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Figure 2: Lifetime prevalence of binge eating disorder

World map displaying lifetime prevalence for BED in % for different countries [18,237-240]. For most countries, only the pooled lifetime prevalence (an average of male and female prevalence) is currently available.

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Comentado [DM1]: Comment for referee:

These will be added to the reference list post peer review.

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Figure 3: Schematic display of pathways of Gut-brain communication. Eating behaviour is regulated by a complex interplay along pathways of brain-gut communication which include structures of the gastrointestinal, endocrine, and central nervous system. Hormonal signalling from the body periphery to brain structures of homeostatic regulation (i.e. the hypothalamus), reward system functioning (i.e. the striatum) and cognitive control (i.e. the prefrontal cortex) plays a crucial role within this communication. Ultimately, these gut-brain cascades influence behavioural outcomes closely tied to the regulation of eating behaviour, such as processes of decision-making and emotion regulation, which have been found to be altered in individuals suffering from BED.

Figure 4: Food intake regulation.

Different peptide hormones, including e.g. ghrelin, leptin and insulin, promoting hunger and satiety signals are directly secreted from the gastrointestinal tract and predominantly communicate to brain regions involved in homeostatic regulation and reward system functioning. Research on alterations in gut-brain communication in BED is yet in its infancy, however, it has been hypothesized that putative dysregulated peptide hormone functioning could be associated with altered hunger-satiety signalling in individuals suffering from BED.

Figure 5: Brain circuits involved in the pathopsychology of BED.

Neuropsychological impairments of BED are meanwhile explored in several brain imaging studies. The neurological basis of binge eating is composed of the hypothalamus (green H in the figure) that is regulating energy balance, e.g. food intake stimulated by gut hormones, the reward system that is representing motivational-affective functions (red shaded in the figure, Am, Nac, VTA, VS, OFC), and cortical regions that are responsible for inhibitory control processes (blue in the figure, PFC, DLPFC, ACC; insula and inferior frontal gyrus not shown). These three systems interact while binge eating episodes and mirror main components of impulsivity, i.e. reward sensitivity and inhibitory control.

ACC anterior cingulate cortex, Am Amygdale, H Hypothalamus, Nac nucleus accumbens, VTA ventral tegmental area, VS ventral striatum, OFC orbitofrontal / ventromedial prefrontal cortex, PFC prefrontal cortex, DLPFC dorsolateral prefrontal cortex (DLPFC).

Box 1: ICD-11 criteria for BED

Binge eating disorder is characterized by frequent, recurrent episodes of binge eating (e.g., once a week or more over a period of several months). A binge eating episode is a distinct period of time during which the individual experiences a subjective loss of control over eating, eating notably more or differently than usual, and feels unable to stop eating or limit the type or amount of food eaten. Binge eating is experienced as very distressing, and is often accompanied by negative emotions such as guilt or disgust. However, unlike in bulimia nervosa, binge eating episodes are not regularly followed by inappropriate compensatory behaviours aimed at preventing weight gain (e.g., self-induced vomiting, misuse of laxatives or enemas, strenuous exercise).

1

Box 2: Medications that have been tested in at least one randomised controlled clinical trial in BED.

Antidepressants	CNS stimulants	Anticonvulsants	Anti-Obesity Medications	Other medications	Combination treatments
Bupropion	Armodafinil	Lamotrigene	D-Fenfluramine	Chromium Picolinate	Phentermine + topiramate
Citalopram	Atomoxetine	Topiramate	Orlistat	Acamprosate	Phentermine + fenfluramine*
Duloxetine	Lisdexamfetamine	Zonisamide	Rimonabant *	ALKS-33	Phentermine + fluoxetine
Escitalopram	Methylphenydate		Sibutramine *	Baclofen	Naltrexone + bupropion
Fluoxetine				Dasotraline *	
Fluvoxamine				GSK 1521498	
Sertraline					
Vortioxetine					

*Medication has been discontinued.

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Box 3: Patient's perspective

Could you describe a typical binge eating episode?

"So, for me, my binges are triggered by negative emotions, so when I feel bad or when I am lonely. (…) And then all of a sudden, the entire pastry was gone and I was totally - I hadn't even noticed, because I lost track of it. Immediately afterwards, I usually felt better (…). But then as time went by, I felt much worse than before, because first you are physically full from overeating, and then also because you have, uhm, a guilty conscience (…)."

How has BED affected your life overall?

"It was especially like, you were constantly preoccupied with food, and were also always checking "do I have anything to eat?". (…) But then of course, there was also the constantly guilty conscience, uhm, because you would always be eating and then accordingly having these [guilty] thoughts, and that was a pretty big burden in [my] day-to-day life."

What caused you the most significant distress?

"The guilty conscience, the negative thoughts. Because you then always completely question your own identity, and you can't look at this in isolation anymore, i.e. only in relation to eating. (…)

[My weight] was a huge burden [as well]. Especially because over time it was impacting [my] physical health as well, through hip problems and shortness of breath, so that you could notice that you couldn't keep up with friends during walks or sport. Which is all very stressful."

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