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Abstract

Objective: In 2015, the Academy for Eating Disorders (AED) collaborated with international patient, advocacy, and parent organizations to craft the “Nine Truths About Eating Disorders.” This document has been translated into over 30 languages and has been distributed globally to replace outdated and erroneous stereotypes about eating disorders with factual information. In this paper, we review the state of the science supporting the Nine Truths. Methods: The literature supporting each of the Nine Truths was reviewed, summarized, and richly annotated. Results: Most of the Nine Truths arise from well-established foundations in the scientific literature. Additional evidence is required to further substantiate some of the assertions in the document. Future investigations are needed in all areas to deepen our understanding of eating disorders, their causes, and their treatments. Conclusions: The “Nine Truths About Eating Disorders” is a guiding document to accelerate global dissemination of accurate and evidence-informed information about eating disorders.
The Science Behind the Academy for Eating Disorders’ Nine Truths About Eating Disorders

Eating disorders are serious mental illnesses that affect millions of individuals worldwide regardless of race, age, nationality, or sex and incur considerable personal, familial, and societal costs. The cumulative lifetime risk by age 80 of anorexia nervosa (AN), bulimia nervosa (BN) and binge-eating disorder (BED) approximates 4.6% (Hudson, Hiripi, Pope, & Kessler, 2007). Inclusion of subthreshold eating disorder behaviors raises this estimate to nearly 10%. Despite the prevalence and toll that eating disorders exact on society, we lack comprehensive understanding of the etiology of eating disorders. We face significant limitations in our ability to prevent, detect, and treat this class of disorders. Stigma surrounding eating disorders has overshadowed the field for decades and has perpetuated misconceptions about their causes, hampered efforts at advancing knowledge, and misdirected lay understanding of these conditions. Perhaps most importantly, stigma surrounding eating disorders has prevented those in need from seeking help (Ali et al., 2017).

In May 2015, the Academy for Eating Disorders (AED) and several international advocacy organizations issued a document entitled “Nine Truths About Eating Disorders” (http://www.aedweb.org/index.php/25-press-releases/163-press-release-aed-releases-nine-truths-about-eating-disorders?quot). The AED focused on presenting truths rather than dispelling myths to introduce empirical evidence into the general knowledge base about eating disorders. The document has been translated into over 30 languages and is being disseminated worldwide to transform perceptions and understanding of eating disorders. In this paper, we present an overview of the empirical foundation upon which the Nine Truths rest to foster a more accurate understanding of the current state of scientific knowledge about eating disorders for patients, families, professionals, and the public.
The truths span a broad literature. In addition to the review of empirical studies, we also attend to modern theoretical and conceptual models and authoritative reviews to evaluate the current state of the science behind the *Nine Truths*. For each truth, we present supporting statements and a strength of evidence rating (Low, Moderate, or High; see Supplementary Table S1 & S2). A detailed summary of the evidence is presented in Supplementary Table S2. In addition to these tables, online supplementary materials provide a rich source of background information and all references for the main text presented there as an annotated bibliography.

**Truth #1: Many people with eating disorders look healthy, yet may be extremely ill.**

1.1 *Eating disorders are associated with significant somatic, psychosocial, and psychological risk.*

Eating disorders are associated with somatic complications in multiple organ systems including the cardiovascular, gastrointestinal, musculoskeletal, dermatologic, endocrine, hematological, and neurological systems (Mehler & Brown, 2015; Mehler & Rylander, 2015; Thornton et al., 2017) as well as psychiatric comorbidities (see Supplementary Table S3). The more chronic and severe the eating disorder, the greater the likelihood of serious somatic complications (Westmoreland, Krantz, & Mehler, 2016). However, severe complications can emerge at any time during the course of illness (Westmoreland et al., 2016). Furthermore, eating disorders are associated with a number of measurable psychological and neurocognitive traits (see Supplementary Table S4 and Statement 4.2).

1.2 *Most individuals with eating disorders do not appear emaciated.*

Weight loss is a defining characteristic of AN, but not BN or BED. In fact, eating disorders are present in all BMI categories (Duncan, Ziobrowski, & Nicol, 2017; Flament et al., 2015), and AN
is less common than the combined prevalence of other eating disorder diagnoses (Kessler et al., 2013; Lindvall Dahlgren & Wisting, 2016; Qian et al., 2013). On average, the BMI of individuals with AN is lower than the BMI of those with BN, which is lower than the BMI of those with BED. Yet, restrictive eating disorders also occur among normal- and overweight individuals and individuals with BN and BED can be normal weight, overweight, or obese (see 5.4).

1.3 Somatic, psychosocial, and psychological manifestations and comorbidities of eating disorders may be difficult to detect.

Many serious somatic complications of eating disorders are not readily visible to lay observers or recognizable to the affected individual (see Supplementary Table S3). Even experienced healthcare professionals have difficulty accurately identifying complications or may misattribute their causes (Currin et al., 2007b; Currin, Schmidt, & Waller, 2007a; Currin, Waller, & Schmidt, 2009; Gaudiani & Mehler, 2016).

Individuals with eating disorders may fail to report the psychological components of eating disorders or have poor insight into their level of impairment (Dalle Grave, Calugi, & Marchesini, 2008; Griffiths, Mond, Murray, & Touyz, 2015; Nordbø et al., 2012; Santonastaso et al., 2009; Vandereycken, 2006a; Vandereycken, 2006b). However, psychological features are often present, even if at milder levels (Carter & Bewell-Weiss, 2011) with some variation across cultures (Lee, Lee, Ngai, Lee, & Wing, 2001; Pike & Dunne, 2015) and in younger patients (Carter & Bewell-Weiss, 2011; Norris et al., 2014) (see Supplementary Tables S3 & S4). Signs and symptoms of an eating disorder should always be taken seriously and not dismissed or minimized. Immediate attention is warranted, and a comprehensive evaluation should be the first step in treatment planning (American Psychiatric Association, 2006; Hay et al., 2014; National Collaborating Centre for Mental Health, 2004).
1.4 Most individuals with eating disorders do not enter treatment; those who do often do so many years into the course of illness.

Epidemiological studies across the world indicate that only a minority of individuals who meet diagnostic criteria for eating disorders seek treatment (Hoek & van Hoeken, 2003; Hudson et al., 2007; Keski-Rahkonen et al., 2009; Kessler et al., 2013; Preti et al., 2009; Twomey, Baldwin, Hopfe, & Cieza, 2015). Eating disorders thus remain undetected, and, even when detected, may not be viewed as serious issues warranting medical intervention (Keel & Brown, 2010).

Truth #1: Summary and future research directions

Confidence ratings: Moderate (1.3) to High (1.1; 1.2; 1.4) (see Supplementary Table S2)

Looks may deceive, and a healthy appearance and failure to acknowledge the severity of these illnesses can delay help-seeking and detection by friends, family, providers, and even patients themselves. Work is required to push past barriers to detection and care. First, longitudinal research is needed to identify early signs of somatic complications and psychiatric comorbidities in eating disorders. A better understanding of prodromal signs and the illness trajectory will enable early detection. Understanding educational needs for physicians and other front-line providers is necessary for broad dissemination of screening and educational tools. For more information on addressing eating disorders in clinical practice, see the AED Guide to Recognition and Management of Eating Disorders (http://www.aedweb.org/index.php/education/eating-disorder-information/eating-disorder-information-13).

Truth #2: Families are not to blame, and can be the patients’ and providers’ best allies in treatment.

2.1 Biological risk factors contribute to the development of eating disorders.
Modern etiological models of psychiatric illnesses consider the bidirectional risk between biology and environment (see Truth #4 for summary of biological factors). The assertion that parental characteristics or family dynamics are necessary and sufficient for the development of eating disorders (i.e., “families are to blame”) represents an historical and dated model of psychopathology and disregards modern etiological conceptualizations of psychiatric risk. Accordingly, the first part of this truth, “families are not to blame,” is empirically and logically justified. This does not imply that evaluation of family functioning in eating disorders is without merit, as such studies may provide actionable information for providers, caregivers, and patients.

2.2 Prototypical family interaction patterns that exist premorbidly among families with eating disorders have not been identified.

A critical methodological issue continues to plague studies of family functioning in eating disorders. Most studies are correlational/differential in nature, precluding causal interpretation. Moreover, the direction of causality has not been examined. Prospective longitudinal designs are necessary to determine whether interactions among family members exist premorbidly or are a consequence of the illness. Some prospective studies have investigated effects of parent and family functioning in predicting later eating disorder onset with mixed results. For example, some evidence suggests that parental factors predict later eating pathology (Johnson, Cohen, Kasen, & Brook, 2002; Nicholls & Viner, 2009; Shoebridge & Gowers, 2000); however, reviews have not identified consistent patterns of risk associated with parenting styles or family interactions (Campbell & Peebles, 2014; Eisler, 2005; Larsen, Strandberg-Larsen, Micali, & Andersen, 2015; le Grange, Lock, Loeb, & Nicholls, 2010; Strober & Humphrey, 1987; Yager, 1982). Indeed, greater family conflict, reduced parental alliance, and increased feelings of depression in families with a child suffering from AN might reflect an accommodation process in response to a severe
and life-threatening condition (Sim et al., 2009). Investigations of parental factors have also been limited by lack of controls with other psychiatric disorders, measurement inconsistencies, and lack of statistical power. For example, certain adverse familial experiences such as sexual abuse may contribute to the risk of pathology in general, and are not eating disorder specific (Kendler et al., 2000).

2.3 Eating disorders place stress on families.

Studies on the experience of caring for a patient with an eating disorder suggest a significant burden and negative impact on the health and well-being of caregivers—especially among mothers and partners (Anastasiadou, Medina-Pradas, Sepulveda, & Treasure, 2014; Kyriacou, Treasure, & Schmidt, 2008). Those caring for patients with AN have reported higher levels of distress than individuals caring for patients with psychoses (Treasure et al., 2001). Parents can initially perceive starvation to be deliberate, which evokes a strong emotional response, significant distress, and can lead to desperate responses in parents in the absence of clear guidance (Whitney et al., 2005). Attributions for these responses should consider the parent’s desire to cease the starvation and save their child. Thus, assisting families in developing tools to deal effectively with an eating disorder is imperative. Distress associated with an eating disorder often extends beyond the identified patient. Stresses associated with having a psychiatrically ill child or partner, coupled with the responsibility for collaborating with providers in the treatment of individuals with eating disorders, underscore the importance of self-care for caregivers (Patel, Wheatcroft, Park, & Stein, 2002; Treasure & Nazar, 2016).

2.4 Family-based treatments have demonstrated effectiveness for the treatment of adolescent AN.
Families and support systems are needed as patient allies during treatment (le Grange et al., 2010). The entire family is affected when dealing with chronic and severe illnesses such as AN. Familial organizational changes that emerge may serve to maintain AN and limit access to adaptive resources the family possesses that are necessary to help overcome the eating disorder (Cook-Darzens, 2016; Eisler, 2005). Family-based treatment (FBT), whereby parents reassert control over the child’s eating, is a promising approach to the treatment of adolescent AN and has some empirical support for the treatment of adolescent BN (Couturier, Kimber, & Szatmari, 2013; le Grange, Lock, Agras, Bryson, & Jo, 2015). FBT helps families recognize resources and knowledge they possessed prior to the onset of the disorder and re-implement them in the family system (Lock & le Grange, 2015). FBT is recommended by many national guidelines for the treatment of eating disorders in youth (Watson & Bulik, 2013) (see Supplementary Table S5).

The role of the family is also important for adults with eating disorders. Partners can be an asset in treatment of adults since they typically express a strong desire to help, yet fear that anything they do or say will inadvertently exacerbate the situation (Treasure & Nazar, 2016). Couple-based interventions for eating disorders leverage the power of relationships and engage the partner in the recovery process (Bulik, Baucom, Kirby, & Pisetsky, 2011; Kirby, Runfola, Fischer, Baucom, & Bulik, 2015; Schmidt et al., 2013). Initial results of couple-based interventions are promising and suggest that close support from a family member enhances treatment regardless of patient age. However, much of family and couple-based intervention research has focused on patients with AN; additional studies are required to confirm the benefit of engaging family members in the treatment of BN and BED (see Supplementary Table S5).

Truth #2: Summary and future research directions

Confidence ratings: Moderate (2.2; 2.3) to High (2.1; 2.4) (see Supplementary Table S2)
In summary, typical patterns of family functioning or structure that give rise to eating disorders have not been identified. This is consistent with the AED position paper on the role of the family in eating disorders (Le Grange et al., 2010). Families are not to blame and in most cases can be the patients’ and providers’ best allies in treatment.

Research on family functioning has been summarized (Larsen et al., 2015; Saltzman & Liechty, 2016). These reviews point to the need for rigorous prospective designs to help understand how environmental variables, including family systems, may interact with biological risk (as discussed in Truth #7 & #8) to either heighten risk or buffer against the development of eating disorders. Eating disorders place stress on a family system, and future investigations that aim to reduce the burden on caregivers are necessary. Consideration of in-home care may be a useful direction for services. Finally, families represent an important base of support for those in recovery, and the effectiveness of family-based treatments for adolescents highlights how parents and caregivers can be important allies in treatment. Future studies that build on this success by examining how families can be best integrated into care of older adolescents, adults, and those who binge eat are of great interest.

Truth #3: An eating disorder diagnosis is a health crisis that disrupts personal and family functioning.

3.1 Eating disorders interfere with personal and family functioning. 3.2 Eating disorders produce financial burden. 3.3 In adolescence, eating disorders may lead to functional impairment and delays in healthy development. 3.4 In adulthood, eating disorders may interfere with intimate relationships, reproductive health, parenting, and health-related quality of life.
Truth #3 is covered by statements in several other Truths. As discussed in Truth #1, an eating disorder represents a health crisis that affects every aspect of an individual’s life. In addition to myriad psychiatric and somatic complications and comorbidities enumerated in Truth #1, eating disorders also lead to considerable psychological distress, as well as isolation, stigmatization, and difficulties with family and other interpersonal relationships (Ali et al., 2017; Caslini et al., 2016; Dimitropoulos, McCallum, Colasanto, Freeman, & Gadalla, 2016; van Langenberg, Sawyer, Le Grange, & Hughes, 2016). Further, eating disorders are associated with financial burden, delays in healthy development, functional impairment, and may interfere with social role functioning including intimate relationships, reproductive health, and parenting (see summaries in Supplementary Tables S2-4).

**Truth #3: Summary and future research directions**

*Confidence ratings: Moderate (3.3; 3.4) to High (3.1; 3.2) (see Supplementary Table S2)*

Eating disorders clearly represent a health crisis (see Truth #1); the effects of which disrupt functioning beyond immediate complications of the eating disorder. Financial burden of eating disorders are significant, and they affect all areas of social and economic well-being, along with delaying or preventing healthy childhood and adolescent development. Future investigations that examine the true cost of eating disorders over the long-term are warranted. Longitudinal studies of eating disorders, including intervention studies, are encouraged to include secondary outcomes related to healthy development in youth, education, finances, employment, reproductive health, and overall quality of life. Further, an empirical review of the literature on relationship, role functioning, and quality of life in eating disorders would advance understanding of how eating disorders influence these vital, but understudied, outcomes.
Truth #4: Eating disorders are not choices, but serious biologically influenced illnesses.

4.1 Disordered eating behaviors can be guided by biological processes associated with automatic (unconscious) events.

In vulnerable individuals, biological drives towards automaticity can provoke rigid habits to the point where individuals struggle to regain control over their dysregulated eating and physical activity (Steinglass & Walsh, 2016). For example, altered inhibitory control, the ability to refrain from engaging in prepotent automatic responses, has been shown across eating disorders subtypes (Collantoni et al., 2016; Galimberti, Martoni, Cavallini, Erzegovesi, & Bellodi, 2012) with the greatest support for bulimic subtypes (Lavagnino, Arnone, Cao, Soares, & Selvaraj, 2016; Wu, Hartmann, Skunde, Herzog, & Friederich, 2013) (see Supplementary Table S4 for a review of traits). Such findings are supported by a position paper that reviewed literature identifying alterations in neurobiological pathways related to reward and self-control associated with eating disorders (Wierenga et al., 2014). Further, a recent theoretical model identifies eating behaviors in AN as habitual behaviors, similar to compulsions in obsessive compulsive disorder, supported by case-control studies on neuropsychological and neuroimaging tasks (Godier et al., 2016; Steinglass & Walsh, 2016). Evidence from animal studies and human neuroimaging also supports some shared neurobiology in eating disorders and other habit-related disorders, including addiction (Kaye et al., 2013b; O’Hara, Campbell, & Schmidt, 2015).

4.2 Biologically-influenced, fundamental personality traits and cognitive styles are associated with eating disorders.

Eating disorders are consistently associated with fundamental personality traits and cognitive styles. These traits are influenced by genetic factors, exist premorbidly, become exacerbated during acute stages of illness, persist after recovery, and/or may affect the prognosis of eating
disorders. Some implicated traits are shared across disorders (e.g., weak central coherence, altered reward sensitivity, anxiety, difficulty with set shifting, altered interoceptive awareness), whereas others are more differentially associated with specific eating disorder phenotypes (e.g., harm avoidance in AN, negative urgency in BN) (see Supplementary Table S4 for overview of associated traits). Overall, identification of genetically influenced personality traits and cognitive styles may reveal core biological risk factors for the development of eating disorders.

4.3 Individuals with eating disorders may experience non-typical responses to eating and activity.

Individuals with eating disorders may have distinct responses to energy restriction and food consumption. For example, individuals with AN may have a paradoxical response to negative energy balance (i.e., taking in less energy than one expends, (Bulik, 2016), such that caloric intake is associated with dysphoric mood (Frank, 2012), whereas caloric restriction evokes a calming, anxiolytic, or euphorogenic effect (Bulik, 2016; Kaye, 2008; Kaye, Wierenga, Bailar, Simmons, & Bischoff-Grethe, 2013a). Non-typical responses to other behaviors such as physical activity and purging (as both positively and negatively reinforcing) are also reported in individuals with eating disorders (Berg et al., 2013; Giel et al., 2013; Kaye, 2008; Klein et al., 2010). Such processes highlight alterations from typical experiences of reinforcement as relevant to development and maintenance of eating disorders, and such patterns may be driven by variations in neurobiology.

4.4 Eating disorders are associated with dysregulation in neurotransmitter availability and function.

Although the precise underlying neurobiology is not fully understood, findings of positron emission tomography (PET) and single-photon emission computed tomography (SPECT) implicate dysregulation in both dopaminergic (DA) and serotonergic (5-HT) systems in eating
disorders (Culbert, Racine, & Klump, 2015; Kaye et al., 2013a; Kaye et al., 2013b; Kaye, 2008; Kessler, Hutson, Herman, & Potenza, 2016; Spies, Knudsen, Lanzenberger, & Kasper, 2015). These systems are central in rewarding aspects of food, motivation, executive functions, and the regulation of mood, satiety, and impulse control.

4.5 Brain structure and function differ between those with active eating disorders and unaffected individuals.

Both human and animal studies have addressed the role of brain anatomy and function in eating disorder psychopathology through use of brain imaging techniques. Studies revealing deviations in structure, function, and activation in the brains of individuals with eating disorders are reviewed comprehensively in several publications (Frank, 2013; Frank, 2015a; Kaye, 2008; O’Hara et al., 2015; Seitz et al., 2014; Seitz, Herpertz-Dahlmann, & Konrad, 2016; Titova, Hjorth, Schiöth, & Brooks, 2013; Van den Eynde et al., 2012).

Structural neuroimaging studies in eating disorders have predominantly shown grey matter reductions in various brain regions that are most pronounced in patients with AN (Seitz et al., 2016). Associations with nutritional abnormalities have been repeatedly demonstrated and in AN volume reductions tend to quickly normalize with weight gain (Bernardoni et al., 2016; Seitz et al., 2016). Functional and structural neuroimaging studies in eating disorders provide evidence that aberrant frontostriatal neural circuitry may represent altered reward pathways, manifesting in impaired regulation of appetite, emotion, and self-control (Frank, 2015b; Friederich, Wu, Simon, & Herzog, 2013; Kaye, Wagner, Fudge, & Paulus, 2011; Kessler et al., 2016; Marsh et al., 2009; Marsh, Maia, & Peterson, 2009). Specifically, altered functioning of limbic regions together with either reduced or exaggerated ‘top-down’ cognitive control (via the prefrontal cortex) are seen as contributing to impulsive (e.g., BN, BED) or exaggerated self-control (e.g., AN) related
symptoms/behaviors (Ehrlich et al., 2015; Friederich et al., 2013; Hege et al., 2015; Kaye & Strober, 2009; Kessler et al., 2016; King et al., 2016; Marsh et al., 2009; Sanders et al., 2015). Neuroimaging and behavioral findings suggestive of alterations in reward pathways have been shown across eating disorders (see Frank, 2015a for review). Findings are mixed regarding the direction of change and the subregions of the brain reward system, likely due to research design issues such as failure to control for nutritional and medication status, exercise, comorbidity, and inadequate sample sizes (Frank, 2015a).

The persistence of core eating disorder psychopathology may reflect not only preexisting neurobiological vulnerabilities, but also neuroadaptation (Treasure et al., 2015), whereby changes may occur in the brain as a consequence of prolonged eating disorder behaviors (e.g., binge eating or restriction). Adolescence, in particular, is associated with a host of neuronal changes, such as increased synaptogenesis, pruning, and myelination of frontal and limbic areas, which are involved in emotional processing and cognition (Benes, 1998; Blakemore & Choudhury, 2006; Tau & Peterson, 2010). A maturing brain may be particularly vulnerable to the insults caused by extreme food restriction or excessive exercise resulting in negative energy balance or highly variable energy consumption (binge-fast cycles).

Evidence from brain structure and function, though preliminary, advances support for the assertion that eating disorders are biologically influenced. Brain structure and function appears to be altered in the active disease state, though the exact nature and stability of differences requires further investigation. Even if brain structure and function differences only occur after an initial shift in eating behavior, these changes may highlight biologically-driven maintenance patterns that impede recovery.

**4.6 Feeding and activity behavior is biologically regulated in animals.**
Animal models shed light on highly specific brain pathways implicated in eating disorder features, including restriction and binge eating. Controlled experiments have led to the development of animal models of hunger (Atasoy, Betley, Su, & Sternson, 2012) and binge eating (Murray, Tulloch, Chen, & Avena, 2015), providing evidence of neurobiological origins of eating disorders. In addition, an activity-based anorexia (ABA) rodent model highlights increased physical activity and reduced body weight in response to restricted food access in animals (Chowdhury, Chen, & Aoki, 2015). Using neural circuit-level approaches that enable activation or inhibition of anatomically and genetically defined brain pathways, like optogenetics and chemogenetics, multiple pathways have been identified that regulate different patterns of feeding behavior (Hardaway, Crowley, Bulik, & Kash, 2015; Sternson & Roth, 2014) (see Supplementary Table S7 for specific regions and nuclei). This approach elevates understanding of how discrete neural circuits control feeding and metabolism, and provides additional evidence of how feeding behavior may be biologically influenced. Further study is needed to determine whether these are therapeutic entry points into pathological models of eating disorders.

4.7 Endocrine changes are associated with eating disorder risk.

The risk for eating disorders increases during reproductive milestones (e.g., puberty, pregnancy) and sex hormones play a role in this risk (Baker, Girdler, & Bulik, 2012; Klump, Keel, Sisk, & Burt, 2010). For example, AN in females typically develops around puberty and is rare before the pubertal transition. Earlier pubertal timing is also associated with increased eating disorder symptoms. Increases in estrogen at puberty are hypothesized to activate genes that influence eating disorder development (Culbert et al., 2015; Culbert, Racine, & Klump, 2016; Klump et al., 2010). The increased risk for eating disorder symptoms at puberty is not surprising given that puberty in females involves considerable changes not only in sex hormones, but also in body composition.
and in neuropeptides that modulate metabolism (Loomba-Albrecht & Styne, 2009; Siervogel et al., 2003).

Pregnancy has also been suggested as both a risk and protective period for eating disorder symptoms. Women with acute AN and BN often report symptom improvement or remission during pregnancy, whereas pregnancy increases risk for relapse for those in remission from AN (Kimmel, Ferguson, Zerwas, Bulik, & Meltzer-Brody, 2016). Pregnancy may also mark a vulnerable time for BED onset (Bulik et al., 2007). Eating disorder symptoms fluctuate across the menstrual cycle in a manner that mirrors changes in sex hormones (Baker et al., 2012; Edler, Lipson, & Keel, 2007; Klump, Keel, Culbert, & Edler, 2008; Racine et al., 2012). Paralleling these findings, a direct association between diminishing estrogen and increasing progesterone levels and eating disorder symptoms has been observed (Edler et al., 2007; Klump et al., 2008). The menopause transition, which involves prolonged and erratic changes in sex hormones, may represent an additional vulnerability period for the development or re-emergence of an eating disorder (Baker & Runfola, 2016; Mangweth-Matzek et al., 2013).

Much less is known about the role of reproductive milestones and sex hormones in the risk for eating disorders in males. Some studies suggest that boys who experience either early or late puberty are at increased risk for eating disorder symptoms (Ricciardelli & McCabe, 2004). Testosterone may be a protective factor against eating disorder development, but findings are inconclusive (Baker et al., 2012).

In addition, aberrant blood and cerebrospinal fluid levels of various appetite-regulating peptides have been observed in individuals suffering from AN or BN (Monteleone & Maj, 2013). Most of these studies, however, are limited both by small sample sizes and their sampling process because plasma levels of appetite-regulating peptides may not reflect the concentrations in the
central nervous system. Serum leptin levels have also been tied with eating disturbances. Serum leptin levels correspond with fat mass in healthy, energy-balanced humans (Hebebrand, Muller, Holtkamp, & Herpertz-Dahlmann, 2007). As would be expected due to their low BMI and fat mass, in acute stages of the illness, individuals with AN generally have low serum leptin levels (Föcker et al., 2011). The observed levels in AN are typically lower than those in BMI-matched healthy lean individuals, most likely due to differences in fat mass (Hebebrand et al., 2007). Intriguingly, hypoleptinemia in AN has also been associated with characteristic hyperactivity (Ehrlich et al., 2009; Holtkamp et al., 2006). Hypoleptinemia is considered to be a state biomarker for AN and together with BMI may represent a useful diagnostic test to distinguish constitutional thinness from AN (Föcker et al., 2011). Additional endocrine changes observed in eating disorders are presented in Supplementary Table S3.

**Truth #4: Summary and future research directions**

*Confidence ratings: Moderate (4.3; 4.4; 4.7); Moderate to High (4.1); High (4.2, 4.5; 4.6) (see Supplementary Table S2)*

The precise nature of underlying biological signatures is an active area of investigation and evidence in support of Truth #4 is accumulating rapidly. In-depth work concentrating on personality traits, cognition, neurobiology, brain anatomy and function, endocrinology, genomics and other -omics (see Truths #7 and 8) contributes to improved understanding of the biological underpinnings of eating disorders. Future research directions for this truth include: 1) examining neuropsychologically-based treatment approaches and outcomes; 2) treatment matching based on phenotypic psychobiological profiles; 3) evaluation of childhood behavioral and neurobiological traits; 4) systematic reviews on altered response to food and exercise in eating disorders and brain
function; 5) additional investigation of neurotransmitter availability and function in eating disorders using methods including postmortem brain analyses, measures of cerebrospinal fluid, PET imaging, and magnetic imaging spectroscopy; 6) basic science and animal research to further probe neural circuitry associated with eating disorder risk; and 7) further examination of the role of longitudinal endocrine changes in eating disorders, including the menopause transition along with the role of hormonal changes in men’s eating disorder risk.

**Truth #5: Eating disorders affect people of all genders, ages, races, ethnicities, body shapes and weights, sexual orientations, and socioeconomic statuses.**

**5.1 Eating disorders affect both males and females.**

Since research on eating disorders has historically focused on women, the nosology of eating disorders has evolved based on female symptom profiles (Anderson & Bulik, 2004) and normative data on males are lacking (see Supplementary Figure S1 for lifetime prevalence of eating disorders by sex). Available evidence suggests that males may also be less likely to seek treatment (Striegel, Bedrosian, Wang, & Schwartz, 2012), less likely to be diagnosed with an eating disorder even when presenting with identical symptoms as females (Currin et al., 2007a), and less likely to access treatment even with similar clinical severity (Austin et al., 2008).

**5.2 Eating disorders occur across the lifespan.**

The typical age of onset of both AN and BN is in adolescence or early adulthood (Currin, Schmidt, Treasure, & Jick, 2005; Keski-Rahkonen et al., 2007; Keski-Rahkonen et al., 2009; Smink, van Hoeken, & Hoek, 2012; Zerwas et al., 2015). Childhood-onset AN is seen clinically from about age 7 years upwards, whereas BN before puberty is quite rare (Nicholls & Bryant-Waugh, 2009). Likewise, BED often begins in late adolescence or early adulthood (Hudson et al., 2007; Kessler...
et al., 2013; Mustelin, Raevuori, Hoek, Kaprio, & Keski-Rahkonen, 2015; Preti et al., 2009), though some people report that they began binge eating early childhood—even before going on their first diet (Grilo & Masheb, 2000). Overall, however, BED commonly begins later than AN and BN, with new cases steadily arising up to age 40-60 years in the population (Hudson et al., 2007; Preti et al., 2009).

Eating disorders in midlife are either recurring or persisting early-onset disorders or new late-onset disorders (Baker & Runfola, 2016; Gagne et al., 2012; Peat, Peyerl, & Muehlenkamp, 2008). Bulimic symptoms in particular are relatively common in midlife women (Baker et al., 2017; Gagne et al., 2012), with one study finding that, among 2,000 women above age 50, 13% endorsed an eating disorder symptom (Gagne et al., 2012). Although the etiology of midlife eating disorders remains poorly understood, life events such as divorce, loss of family members, or somatic illness could serve as triggers (Kally & Cumella, 2008; Peat et al., 2008), and pregnancy or menopause with accompanying biological changes may increase vulnerability for onset or recurrence of eating disorders (Baker & Runfola, 2016; Baker et al., 2017; Bulik et al., 2007; Peat et al., 2008). Very little is known about eating disorders in men in midlife and beyond.

5.3 Eating disorders occur in all races and ethnicities.

A review of community studies from 30 countries found no systematic association between ethnicity/race and eating disorder occurrence (see Supplementary Figure S2) (Mitchison & Hay, 2014). Although eating disorders were initially considered to be limited to Western culture, accumulating evidence ties eating disorders more generally to economic development, urbanization, and industrialization across the globe (Pike, Dunne, & Addai, 2013; Pike, Hoek, & Dunne, 2014). Rising incidences of eating disorders have been reported in numerous countries, particularly in Asia and the Middle East (Pike & Dunne, 2015; Pike et al., 2014). In the United
States, the prevalence of eating disorders in ethnic and racial minority groups is similar to non-Latino whites, while ethnic minority groups more frequently report binge-eating behavior compared with non-Latino whites (Marques et al., 2011). AN has been found to be somewhat less common among Black than White Americans (Pike et al., 2013; Striegel-Moore & Franko, 2003). Importantly, racial and ethnic minorities are underrepresented in specialist eating disorder services, possibly due to underdetection in primary care (Striegel-Moore et al., 2003).

5.4 Eating disorders occur in individuals of all shapes and sizes.

Weight and BMI can vary substantially across the different types of eating disorders. In a sample of over 3,000 adolescents, eating disorders were present in all BMI categories (Flament et al., 2015). Restrictive eating disorders in normal- and overweight individuals are increasingly being acknowledged. The DSM-5 facilitates the diagnosis of atypical AN in individuals who meet all criteria for AN with the exception of low weight (American Psychiatric Association, 2013). This diagnosis is appropriate, for example, in individuals who begin at high weights and lose weight precipitously. A substantial portion of treatment-seeking adolescents with restrictive eating disorders have a history of overweight or obesity (Lebow, Sim, & Krausdorf, 2015), and there is a well-established relationship among dietary restriction, obesity, and eating disorders (Field et al., 2003; Neumark-Sztainer et al., 2006). In a review of clinical trials of BN, baseline BMI was most commonly in the normal range (Berkman et al., 2006), whereas community studies indicate that BN is prevalent in overweight and obese adolescents (Flament et al., 2015) and predicts weight gain over time (Fairburn, Cooper, Doll, Norman, & O’Connor, 2000; Micali et al., 2015). Individuals with BED are commonly overweight or obese (Hudson et al., 2007; Kessler et al., 2013), yet a substantial minority of individuals with BED are normal-weight, particularly early in
the course of illness (Fairburn et al., 2000; Mustelin et al., 2015) (see Statement 1.2 for additional information on BMI and eating disorders).

5.5 Eating disorders are present across different sexual orientations and gender identities.

Homosexual orientation is regarded as a risk factor for eating disorders in men: gay and bisexual men report more body dissatisfaction and disordered eating, and are more likely to be diagnosed with an eating disorder than heterosexual men (Brown & Keel, 2012; French, Story, Remafedi, Resnick, & Blum, 1996; Russell & Keel, 2002). In women, the evidence on sexual orientation and disordered eating is mixed. Lower body dissatisfaction among homosexual women have been observed in some, but not all studies (Alvy, 2013; French et al., 1996; Moore & Keel, 2003; Morrison, Morrison, & Sager, 2004). In a population-based cohort of adolescents, unhealthy weight control behaviors (e.g., laxative use, fasting, and vomiting) were significantly more prevalent among sexual minority males and females than in their heterosexual peers (Hadland, Austin, Goodenow, & Calzo, 2014).

Most research on eating-related pathology has focused on cisgender individuals (i.e., those whose gender identity matches the sex they were assigned at birth). A study of over 280,000 American college students indicated that transgender individuals may have particularly high eating disorder risk: 16% of transgender youth reported being diagnosed with an eating disorder in the past year, compared with 2% and 4% of cisgender sexual minority men and women, respectively (Diemer, Grant, Munn-Chernoff, Patterson, & Duncan, 2015). Similarly, studies of Canadian transgender youth and of UK transgender adults have found high rates of endorsement of disordered eating behaviors, particularly among trans males (Watson, Veale, & Saewyc, 2016; Witcomb et al., 2015).
5.6 There is no consistent association between socioeconomic status and risk for eating disorders.

Although higher parental education has been associated with increased risk of being diagnosed with an eating disorder in registry studies (Ahrén et al., 2013; Goodman, Heshmati, & Koupil, 2014), evidence suggests that this association may be genetically rather than socially mediated (Duncan et al., 2017). No consistent association has been observed between socioeconomic status and risk of eating disorders (Mitchison & Hay, 2014). In Australian population surveys, both binge eating and purging increased more in low-income than high-income individuals during a 10-year time period, suggesting an ongoing shift in the demographics of disordered eating (Mitchison, Hay, Slewa-Younan, & Mond, 2014).

Truth #5: Summary and future research directions

Confidence ratings: Moderate (5.5; 5.6); Moderate to High (5.2); High (5.1; 5.3; 5.4) (see Supplementary Table S2)

In summary, no dominant pattern of age, body size, sexual orientation or gender identity, race, ethnicity, or socioeconomic status is associated with eating disorder risk. Providers should remain vigilant to eating disorders in all individuals regardless of demographic characteristics. Further research on socioeconomic status and eating disorders are needed to clarify inconsistent patterns observed and proposed genetic associations.

Longitudinal studies that consider weight trajectories as they relate to eating disorder symptom development are needed, as it is clear that individuals may develop eating disorders from any premorbid weight. More research on eating disorders among sexual minorities is also necessary for the development of targeted prevention and intervention efforts, specifically
longitudinal studies that examine how sexual and gender identity development in youth may impact eating disorder risk.

**Truth #6: Eating disorders carry an increased risk for both suicide and medical complications.**

6.1 **Eating disorders are associated with premature death.**

The most significant medical complication of an eating disorder is premature death. The standardized mortality ratio (SMR) associated with AN ranges between 5.9 and 6.2, meaning the risk of death for individuals with AN is up to 6.2 times greater than the risk in the general population, and the weighted annual mortality rate of AN is reported as 5.1 per 1000 person years (Chesney, Goodwin, & Fazel, 2014; Papadopoulos, Ekbom, Brandt, & Ekselius, 2009). Additionally, for females with AN between the ages of 15-24 years old, the mortality rate is 12 times higher than the death rate of all other causes of death (Klump, Bulik, Kaye, Treasure, & Tyson, 2009). Notably, AN also has one of the highest mortality rates of any psychiatric illness (Chesney et al., 2014), and one in five deaths in AN is attributable to suicide (Arcelus, Mitchell, Wales, & Nielsen, 2011).

The mortality rate for BN is also significantly elevated relative to the general population, with meta-analyses estimating the SMR for BN to be 1.9 (Chesney et al., 2014). For those with BN, mortality risk may increase with severity (Huas et al., 2013). One clinical follow-up study in Finland found the all-cause mortality hazard ratio for BED to be 1.77 (0.60, 5.27) (Suokas et al., 2013). Though similar in effect size to reported SMRs for BN, this hazard ratio for BED was not significant. With the inclusion of BED in the DSM-5, more studies on epidemiology, course, and outcome of BED are likely.
6.2 Risk of suicide is elevated in eating disorders.

The risk of suicide attempts is also elevated in eating disorders. In the Swedish population born between 1979 and 2001, the odds ratio (OR) of suicide attempts was estimated to be 5.3 (95% CI: 5.0, 5.5) for any eating disorder, meaning that the risk of suicide attempts in people with eating disorders is 5.3 times the risk in individuals without an eating disorder. The ORs for suicide were 4.4 (95% CI: 4.1, 4.7) for AN and 6.3 (95% CI: 5.7, 6.9) for BN (Yao et al., 2016). Similar relative risks have been reported in the Danish population for the period between 1989 and 2006 (Zerwas et al., 2015). A large clinical study found that 35.6% of eating disorder patients had attempted suicide at least once, and patients with binge eating and/or purging behaviors were associated with an elevated risk for suicide attempts compared with patients without such behaviors (Fedorowicz et al., 2007; Foulon et al., 2007). In Sweden, 13.6% of women with a lifetime history of BED had at least one lifetime suicide attempt (Pisetsky, Thornton, Lichtenstein, Pedersen, & Bulik, 2013; Runfola, Thornton, Pisetsky, Bulik, & Birgegård, 2014).

Based on a meta-analysis, the suicide-specific SMR is 18.1 (95% CI: 11.5, 28.7) for AN (Keshaviah et al., 2014). Among female AN patients in specialized care, this ratio could be as high as 31.0 (95% CI: 21.0, 44.0) (Preti, Rocchi, Sisti, Camboni, & Miotto, 2011). The suicide-specific SMR is reported as 7.5 (95% CI: 1.6, 11.6) for BN (Preti et al., 2011) and no deaths by suicide in individuals with BED were reported; however, more data for BED are expected to emerge as recognition and reporting of BED increases. Familial co-aggregation of eating disorders and suicide attempt has been observed in nationwide population data (Yao et al., 2016). Two studies from Australia (Wade, Fairweather-Schmidt, Zhu, & Martin, 2015) and Sweden (Thornton, Welch, Munn-Chernoff, Lichtenstein, & Bulik, 2016) have reported that the co-occurrence of eating disorders and suicide may be in part due to shared genetic factors.
Whereas women with disordered eating in the community may be more likely to attempt suicide than males (Davison, Marshall-Fabien, & Gondara, 2014), no sex differences have been found for the risk of suicide attempts or death by suicide in eating disorders (Yao et al., 2016).

**Truth #6: Summary and future research directions**

*Confidence ratings: High (6.1;6.2) (see Supplementary Table S2)*

Increased risk of premature death, including suicide, among eating disorders is well established; however, little is known about the mechanism underlying this association. Future investigations should consider why eating disorders specifically display increased risk for suicide and examine how psychobiological models of suicide (Anestis et al., 2016) may pertain to those with eating disorders, including how unique complications associated with eating disorders, such as nutritional status, may influence risk as proposed by these models.

**Truth #7: Genes and environment play important roles in the development of eating disorders.**

*7.1 Eating disorders run in families.*

Family, twin, and genetic research has established that eating disorders run in families and genes play a role in this familial pattern (Yilmaz, Hardaway, & Bulik, 2015). Familial history of AN increases the risk of AN development fourfold compared with the general population (Steinhausen, Jakobsen, Helenius, Munk-Jørgensen, & Strober, 2015). Furthermore, AN, BN, and eating disorder not otherwise specified (EDNOS) track together in families, suggesting a lack of specificity (Lilenfeld et al., 1998; Strober, Freeman, Lampert, Diamond, & Kaye, 2000). BED also aggregates in families independent of obesity (Fowler & Bulik, 1997; Hudson et al., 2006). Twin studies cannot identify which genes influence risk, but they have identified a strong genetic
contribution in AN, BN, and BED. Specifically, 48-74% of the total variance in liability to AN, 55-62% to BN, and 39-45% to BED is attributable to genetic factors (Yilmaz et al., 2015).

7.2 Genes play a role in eating disorder risk.

Genome-wide association studies (GWAS), which scan the entire genome in a hypothesis-free manner, and related approaches such as exome sequencing and whole genome sequencing have rapidly accelerated the field. The Eating Disorders Working Group of the Psychiatric Genomics Consortium (PGC-ED) recently identified the first genome-wide significant locus for AN (Duncan et al., 2017) in an area that harbors genes previously implicated in type 1 diabetes and other autoimmune disorders. We expect this will mark an inflection point in genomic discovery if AN follows the same progression of findings as other psychiatric disorders such as schizophrenia, where increased sample size has led to fruitful genomic discovery (Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014). GWAS represent a starting point for genomic discovery, as post-GWAS science reveals causative biological pathways and the functional significance of implicated genes and epigenetic enhancer regions. No GWAS of BN or BED have been conducted to date. In addition to GWAS approaches, familial linkage analysis with whole-genome and exome sequencing has identified two potential missense mutations (Cui et al., 2013), which evidence a connection with eating-disordered behaviors in a recent mouse model (Lutter et al., 2017).

7.3 Environmental factors play a role in eating disorder risk.

Genes do not act alone: environment plays an important role. Cross-sectional and longitudinal twin studies also indicate that nonshared environmental factors account for variance in eating disorder symptoms. Cultural pressure for thinness has been identified as a specific risk factor for eating disorders, and clinical trials of interventions that reduce thin-ideal internalization have led to
reductions in eating disorder symptoms (Culbert et al., 2015). While thin-ideal internalization may have some genetic influence, one longitudinal twin study indicates that nonshared environmental influences were most important in the etiology of thin-ideal internalization (Suisman et al., 2014).

**7.4 Only a small portion of individuals exposed to environmental risk develop eating disorders.**

Dieting, drive for thinness, and portion size escalation are widespread in industrialized countries and may represent risk scenarios for the development of eating disorders (Jacobi, Hayward, de Zwaan, Kraemer, & Agras, 2004; Steenhuis & Vermeer, 2009; Striegel-Moore & Bulik, 2007); however, despite nearly ubiquitous exposure, threshold illnesses are disproportionately rare. A current hypothesis is that individuals genetically predisposed to eating disorders are most vulnerable to societal pressures and environmental insults. Eating disorders are “complex traits,” meaning that multiple genetic and environmental factors—each of small to moderate effect—act together to increase risk. Genetic and environmental factors may not only act in an additive manner, but may co-act in other ways (see Truth #8).

**Truth #7: Summary and future research directions**

*Confidence rating: Moderate (7.4); Moderate to High (7.1); High (7.2; 7.3) (see Supplementary Table S2)*

Genomic discovery in AN is accelerating rapidly, but work on BN and BED is woefully behind. Very large sample sizes (in the tens of thousands) are key to discovering genetic variants associated with risk, and global cooperation is underway to achieve such sample sizes. Advances in genetic methodology, coupled with increasing knowledge about environmental risk factors, will provide a more complete and accurate picture of eating disorder etiology.
Truth #8: Genes alone do not predict who will develop eating disorders.

8.1 Eating disorders do not follow Mendelian transmission patterns.

Inheritance patterns for eating disorders do not follow the traditional Mendelian patterns where variation in one gene results in one disorder (e.g., Huntington’s chorea). Rather, hundreds (or perhaps thousands) of genes act in concert and are influenced by environmental factors. An individual’s risk is a composite of the cumulative number of genetic and environmental risk and protective factors to which they are exposed. This pattern is supported by several case-control studies examining candidate genes that show inconsistent effects (see Yilmaz et al., 2015 for a review).

8.2 Many cases of eating disorders are sporadic, meaning there is no known family member who suffers from an eating disorder.

Family studies indicate that the relative risk for eating disorders is higher in family members of affected individuals; however, the majority of affected individuals have no known affected family members (Bould et al., 2015; Steinhausen et al., 2015; Strober et al., 2000). This literature is limited in that eating disorder history among relatives may not be fully known or accurately captured.

8.3 Genes and environment may co-act to influence risk for eating disorders.

Genes represent probabilities in all complex traits, such as eating disorders. Individuals with a high genetic susceptibility for disordered eating may be protected by other factors, whereas individuals at relatively low genetic risk may be burdened with cumulative or extreme environmental insults leading to possible eating disorder development despite their favorable genetic profile. Understanding the role that genes and environment play in eating disorders requires a deep acceptance of probability and of uncertainty.
Genes and environment may co-act to influence risk for eating disorders (Trace, Baker, Peñas-Lledó, & Bulik, 2013). First, in most families, parents and extended family provide both genes and shared environment, meaning that these two factors are confounded. Second, individuals with a stronger genetic susceptibility for eating disorders might be more sensitive to environmental factors (dieting, bullying, teasing, or overeating). Whereas many adolescents may try dieting, only for a few does it serve as an environmental trigger for an underlying genetic predisposition. Third, an individual who is genetically predisposed to traits associated with eating disorders (e.g., perfectionism, persistence, high physical activity) can seek out environments that may serve as triggers (e.g., sports that have a lean body type ideal, certain social media content) (Carrotte, Vella, & Lim, 2015; Giel et al., 2016; Rousselet et al., 2017). This phenomenon is known as an active gene-environment correlation (Plomin, DeFries, & Loehlin, 1977). Genetic research combined with ambulatory assessment may help understand how environmental influences affect risk for eating disorders by pinpointing specificity of risk factors.

Rigorous studies of gene-environment interaction in eating disorders are sparse. Some developmental twin studies have examined gene-environment interaction (Culbert et al., 2015). For example, contribution of genetic risk to the emergence of dysfunctional eating attitudes and disordered eating varies with developmental stage, with higher genetic effects observed in mid-to-late adolescence and mid-to-late puberty (Culbert et al., 2015; Culbert, Burt, McGue, Iacono, & Klump, 2009; Klump, Burt, McGue, & Iacono, 2007). More sophisticated analytic techniques that examine interplay between genetic risk and family environment provide indication that fit between an individual’s genotype and their family environment may be relevant for eating disorder risk (Culbert et al., 2015). In human studies, large samples using genome-wide and phenome-wide data are required for credible conclusions. Following a report of a rare missense mutation being
associated with the development of eating disorders, Lutter et al. (2017) found that group (vs. individually) housed transgenic female mice displayed irregular feeding and anxiety behaviors, preliminarily revealing both sex-specific and gene by environment effects.

Additional ways in which genes and environment interact are via mechanisms collectively called epigenetics—the modification of DNA, RNA, or proteins by biological or environmental factors. These mechanisms alter gene expression without changing the DNA sequence. Importantly, epigenetic changes such as DNA methylation are tissue specific and can rarely be directly studied in the brain. Therefore, it is important to determine whether epigenetic changes seen in blood are good proxies for epigenetic changes in brain (Walton et al., 2016).

Preliminary epigenetic studies have reported changes in dopaminergic genes and genes for proopiomelanocortin (*POMC*), cannabinoid receptor 1 (*CNR1*, also referred to as *CB1*), atrial natriuretic peptide (*NPPA*, also referred to as *ANP*), alpha synuclein (*SNCA*), and oxytocin receptor (*OXTR*) (Ehrlich et al., 2010; Ehrlich et al., 2012; Frieling et al., 2007; Frieling et al., 2008; Frieling et al., 2010; Kim, Kim, Kim, & Treasure, 2014; Schroeder et al., 2012). If replicated, epigenetic findings could make important contributions to understanding the role of non-DNA elements in eating disorder susceptibility.

**Truth #8: Conclusions and future research directions**

*Confidence ratings: Low (8.2; 8.3); Moderate (8.1) (see Supplementary Table S2)*

A complex interplay between genetic and environmental factors underlies the development of eating disorders. Future research on genetic pathways and their interplay with environmental factors is an exciting and emerging area of research—and one that has the potential to provide key understanding of the multiple and nuanced facets by which individuals may develop eating pathology. In the short-term, large population-based studies with both genotypic and phenotypic
information to probe gene-environment interactions, along with case-control studies to examine potential epigenetic effects represent key areas for advancing knowledge regarding complex risk patterns.

9. Truth #9: Full recovery from an eating disorder is possible. Early detection and intervention are important.

9.1 A substantial portion of individuals with eating disorders achieve recovery.

Full recovery from an eating disorder is not only possible, but indeed probable. A substantial portion of individuals with eating disorders achieve recovery, some without seeking treatment (Eddy et al., 2016; Keel & Brown, 2010; Steinhausen & Weber, 2009; Steinhausen, 2009). Five-year clinical recovery rates have been estimated at 67% for AN (Keski-Rahkonen et al., 2007) and 55% for BN (Keski-Rahkonen et al., 2009) in community samples, and by 10 years after eating disorder onset 70% of individuals are recovered (Berkman, Lohr, & Bulik, 2007). Although recovery is attainable, there is a lack of consensus on the exact definition of recovery, making it difficult to compare recovery rates across studies (Bardone-Cone et al., 2010; Emanuelli, Waller, Jones-Chester, & Ostuzzi, 2012). Traditionally, these definitions focus on physical and behavioral recovery. Physical recovery refers to the resumption and maintenance of a healthy body weight and a normalization of all physical parameters affected by the eating disorder, whereas behavioral recovery means the absence of eating-disorder related behaviors such as food restriction, binge eating, and purging. Psychological recovery, including the attainment of normal attitudes toward food and the body, is important yet often overlooked. It has been proposed that full recovery is achieved only when patients are indistinguishable from healthy controls on all eating disorder related measures, including psychological aspects (Bardone-Cone et al., 2010). Although this definition may seem stringent, it is attainable. Full recovery from an eating disorder is possible,
and given that lingering eating disorder attitudes predict relapse (Helverskov et al., 2010), the psychological component of recovery is clinically relevant.

9.2 Early detection and intervention may improve prognosis.

For some, recovery from an eating disorder is possible without treatment; however, early detection and intervention are preferred for all eating disorders (Treasure et al., 2015). For AN, a longer duration of illness before presentation for treatment is associated with poor outcome (Keel & Brown, 2010; Pike, 1998; Richard, Bauer, & Kordy, 2005), and the probability of recovering decreases as a function of duration of illness, irrespective of treatment (Pike, 1998). For BN, some studies find that a longer duration of illness is associated with poor outcome, whereas others observe that severity of illness and additional psychiatric comorbidities are more significant predictors of outcome (Steinhausen & Weber, 2009). However, in general, the sooner an eating disorder is identified and treatment can begin, the better prognosis there is for full recovery.

9.3 Effective psychological interventions for eating disorders exist. Many, but not all, patients benefit.

9.4 Medication can be an effective treatment component for eating disorders.

Treatment for an eating disorder typically includes psychological treatment and may include medication (Zipfel, Giel, Bulik, Hay, & Schmidt, 2015). For AN, weight restoration is an essential first step in treatment. Inpatient renourishment for AN is typically directed by clinical guidelines that advocate for a “low and slow” approach, due to concerns about refeeding syndrome (Solomon & Kirby, 1990). However, this approach is being challenged in favor of more aggressive renourishment techniques, leading to shorter hospital stays and a favorable safety profile (Garber et al., 2013; Madden et al., 2015; Redgrave et al., 2015). Once medical stabilization of an eating disorder is established, patients may step down to other levels of care. The evidence base has been thoroughly reviewed for psychotherapeutic and medication interventions for eating disorders.
Supplementary Tables S5 & S6 provide an overview of psychotherapeutic and medication treatments.

**Truth #9: Summary and future research directions**

*Confidence Ratings: Low (9.4 for AN); Moderate (9.2); High (9.1; 9.3; 9.4 for BN/BED) (see Supplementary Table S2)*

Increasing understanding of the mechanisms underlying eating disorders will facilitate the development of more effective and personalized prevention and treatment options, eventually leading to increased recovery rates and shorter recovery times. Some evidence-based treatments have proven efficacy. Importantly, recovery from eating disorders can and does occur at any age and for those who do not achieve complete remission, quality of life and somatic status may be improved, monitored, and stabilized (Treasure, Stein, & Maguire, 2015). Future research goals include development of strategies for early detection and intervention, development of a provider’s toolbox that includes psychological and pharmacological interventions that are effective for a range of eating disorders in diverse populations, drug development or repurposing investigations to target core biological pathology of AN, studies of long-term efficacy of medication interventions for all eating disorders, and studies of the effectiveness of medications for eating disorders in community settings.

**General conclusion**

We summarize the available literature that led to the development of the “Nine Truths About Eating Disorders.” Eating disorders are not choices and do affect individuals from all walks of life. They result from a combination of biological (including genetic) and environmental factors. Eating disorders increase the risk for suicide and medical complications, and interrupt personal and family functioning. Families are not to blame and can be critical sources of support in recovery.
Clearly, additional work is needed to better understand risk factors, course of illness, and treatment of eating disorders. Important for advancing science in this area is the ability to remain flexible in thinking about causal factors and acknowledge accumulating evidence underlying these truths to eliminate misconceptions that have plagued the field for decades. In addition, providers should be mindful of the multitude of ways eating disorders can arise and be especially vigilant to signs of somatic and psychiatric complications resulting from AN, BN, and BED. As scientists, providers, patients, family, and friends, we need to continue educating others in the community about these truths in order to detect and treat eating disorders as soon as possible.

Yet, the science of this field cannot be advanced in the absence of appropriate investment and financial support from organizations worldwide that fund research. A 2015 blog post by the former director of the US National Institute of Mental Health, Thomas Insel, MD, revealed how woefully underfunded research on eating disorders was relative to the disability-adjusted life years associated with the illnesses (http://www.nimh.nih.gov/funding/funding-strategy-for-research-grants/white-paper_149362.pdf). Despite the dire morbidity and mortality statistics, eating disorders continue to be low-priority illnesses, we contend, in part due to long-standing misconceptions about their causes and consequences. Funding is required for larger more definitive collaborative studies to avoid the confusion that arises from conflicting results from small, underfunded, underpowered, and unreplicated investigations. Far too often, such small-budget studies are all that investigators can afford to conduct.

Science is constantly evolving, and novel methods will enhance our ability to clarify the etiology of eating disorders and to develop scientifically informed and effective treatments for these debilitating illnesses. With adequate support for science, emerging information will facilitate the refinement of the Nine Truths and may in fact uncover new truths. Ultimately, it is our hope
that dissemination of the *Nine Truths* will serve to reduce stigma and misunderstanding, and, via their impact on science and practice, reduce illness burden, improve quality of life, and eliminate mortality from eating disorders.
Annotated Bibliography


https://doi.org/10.1016/j.eatbeh.2003.07.001

https://doi.org/10.1080/13811118.2015.1048399

https://doi.org/10.1001/archgenpsychiatry.2011.74

Authors meta-analyzed 36 quantitative studies covering the mortality of eating disorders. The weighted mortality rates (i.e., deaths per 1000 person-years) were 5.1 for AN, 1.7 for BN, and 3.3 for EDNOS. The standardized mortality ratios were 5.86 for AN, 1.93 for BN, and 1.92 for EDNOS. One in 5 individuals with AN who died had committed suicide.

https://doi.org/10.1038/nature11270

Demonstration that cell and pathway specific optogenetic activation of a pathway from Agouti related peptide-expressing neurons in the arcuate nucleus to the paraventricular nucleus of the hypothalamus induces hunger.


Authors compared bulimic symptoms in premenopausal and perimenopausal midlife women and examined the association between these symptoms and reproductive and appetite hormones. No mean differences in bulimic symptoms were observed between premenopause and perimenopause. A significant positive association between leptin and binge eating was observed.


Grey matter reductions which are typically found in acutely underweight anorexia nervosa patients were found to be reversed at a rate much faster than previously thought upon successful weight gain.


In a sample of 158,697 children born in Stockholm county 1984-1995, Sweden, the authors tested whether the diagnosis of an eating disorder in a parent was predictive of a diagnosis of an eating disorder in the offspring. Due to low rates of eating disorders in males, analyses were restricted to females who were found to be at increased risk of being diagnosed with an eating disorder.


*Uniting Couples (in the treatment of) Anorexia Nervosa (UCAN) is a couple based intervention founded on cognitive-behavioral couple therapy principles. The authors discuss the delivery of the treatment and highlight its potential to enhance both retention and treatment outcome.*


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*The role of hormonal factors influencing eating disorders is still unknown. However, the strongest evidence for etiologic effects has emerged for ovarian hormones, suggesting that estradiol reduces food intake whereas progesterone and testosterone increase food intake.*


https://doi.org/10.1002/eat.20385


In a sample of nearly 300,000 U.S. college students, transgender and cisgender sexual minority young adults reported a higher prevalence of past-year self-reported eating disorder diagnosis and past-month compensatory behaviors (i.e., self-induced vomiting, diet pills, and laxatives) than their cisgender heterosexual peers.


In a U.S. general population sample, lifetime eating disorder prevalence was 2.22% in men and 4.93% in women. The prevalence of any lifetime and past 12-month ED, binge eating disorder and recurrent binge eating was highest among obese individuals.


First identified genome-wide significant locus for anorexia nervosa on chromosome 12 (rs4622308) in a region harboring a previously reported type 1 diabetes and autoimmune disorder locus. Significant positive genetic correlations observed between anorexia nervosa and schizophrenia, neuroticism, educational attainment, and high-density lipoprotein cholesterol, and significant negative genetic correlations were observed between anorexia nervosa and body mass index, insulin, glucose, and lipid phenotypes.


Edler, C., Lipson, S. F., & Keel, P. K. (2007). Ovarian hormones and binge eating in bulimia nervosa. *Psychological Medicine, 37,* 131-141. [https://doi.org/10.1017/S0033291706008956](https://doi.org/10.1017/S0033291706008956)


*Individuals recovered from anorexia nervosa showed elevated brain activity in the dorsolateral prefrontal cortex (DLPFC) as well as greater functional coupling between the DLPFC and the orbitofrontal cortex during the anticipation phase of a monetary reward paradigm. The findings are suggestive of elevated self-regulatory processes in response to rewarding stimuli in patients recovered from anorexia nervosa.*


In a checklist study, individuals with eating difficulties and clinicians ranked factors associated with recovery. Domains included psychological-emotional-social, weight-controlling behaviors, non-life-threatening and life-threatening features, and evaluation of one's own appearance. Ill individuals and clinicians agreed on the ranking of importance of these factors, but those with eating disturbances, considered 'psychological-emotional-social' and 'evaluation of one's own appearance' criteria as more important to recovery than clinicians.


https://doi.org/10.1016/j.eurpsy.2007.03.004


https://doi.org/10.1517/17530059.2012.673583


https://doi.org/10.1002/(SICI)1098-108X(199603)19:2<119::AID-EAT2>3.0.CO;2-Q


https://doi.org/10.1002/eat.22099


https://doi.org/10.1016/j.jadohealth.2013.07.014


*Exploration of the role of habits, similar to those reported in compulsive disorders, that are hypothesized to play a role in the development and maintenance of anorexia nervosa. In two parallel studies, individuals with the binge/purge subtype of anorexia nervosa, restricting subtype of anorexia nervosa, and individuals recovered from anorexia nervosa did not show reliance on habits compared to healthy controls. Intact goal-directed learning was evident across all subtypes of anorexia nervosa.*


 *Exploration of how stress modulates different forms of feeding in animal models and identification of molecularly defined brain circuits that regulate feeding. Authors discuss the potential impact of these interactions and circuits for eating disorder biology.*


Using a naturalistic design, the authors investigated the 30-months outcome (remission and relapse) of various treatments and predictors of outcome in 629 patients (adolescents and adults) with different eating disorders. Almost half the patients provided data at follow-up of which 42% attained full remission, and 30% partial remission (no longer fulfilling the criteria for an eating disorder diagnosis). A total of 22% or 35% of those obtaining full or partial remission relapsed. Adult patients with AN-like conditions had the poorest outcome, and low BMI emerged as predictor of poor outcome in AN. The frequency of bingeing and purging was a predictor of poor outcome in BN.


The mortality risk of bulimia nervosa was estimated by following 258 individuals admitted to a hospital in France between 1988 and 2004. The mean follow-up duration for subjects was 10.5 years. A total of 10 deaths were recorded during the follow-up time period, with the majority of deaths from suicide. The results show that individuals with bulimia nervosa are at an increased risk for death, specifically suicide.


Decreased activation in frontoparietal regions involved in decision making, but faster and more consistent choice behavior of acute patients with acute anorexia nervosa in a temporal delay.
discounting task, suggests that the altered efficiency of neural resource allocation might underlie an increased level of self-control.

https://doi.org/10.1080/10640266.2015.1044349


Changes in genetic and environmental influences on disordered eating across early-, mid-, and late-adolescence were examined. Significant changes in genetic and shared environmental effects across early- to mid-adolescence were observed. Specifically, genetic factors accounted for a small proportion of variance during early adolescence, but increased in importance and accounted for approximately 50% of the variance in disordered eating at mid- and late-adolescence. Shared environmental influences decreased substantially from early- to mid-adolescence.


In a sample of 198 female adolescent twins, this study explored if estradiol levels moderated disordered eating by comparing twin correlations in low vs. high estradiol groups. They found similar MZ and DZ correlations in the low estradiol group, indicating no genetic effect. In the high estradiol group the MZ twin correlation was more than double the DZ twin correlation indicating genetic effects.


Comprehensive review of the literature on medical complications associated with purging behaviors in bulimia nervosa, focusing on self-induced vomiting and laxative abuse. While complications of laxative abuse involve mainly the gastrointestinal system and electrolyte disturbances, complications of self-induced vomiting also include cutaneous, dental, throat, cardiac, reproductive, and pulmonary domains. Effects are dependent on the mode and frequency of purging.


Using two Australian household surveys, one in 1998 (n=3010) and the other in 2008 (n=3034), the authors interrogated the stereotype that eating disorders are diseases of young, white, socioeconomically privileged women. Between the two samples, the most drastic increases in prevalence of various eating-disorder symptoms were in participants who were male, >45 years old, or from lower socioeconomic brackets. All disordered eating traits had similar negative impact on health-related quality of life regardless of demographic factors.


*In a community sample of young women, lifetime prevalence of DSM-5 BED was 0.7%, mean age of onset was 19 years, comorbid major depressive disorder was common, and BED was frequently preceded by relative overweight in adolescence.*


fare 5 years later? Journal of the American Dietetics Association, 106, 559-568.

https://doi.org/10.1016/j.jada.2006.01.003


https://doi.org/10.1002/erv.1097

In depth-interviews from 36 women with anorexia nervosa were collected to explore what makes individuals with anorexia nervosa ambivalent about recovery. Core obstacles reported by patients with anorexia included: perceiving judgements, feeling stuck, feeling distressed, denying anorexia nervosa, eating, gaining weight, and perceived benefits of the illness.


Examination of the effect of genotype-environment interaction and correlation in behavioral genetic studies (twin and adoption studies).


In a cross-sectional survey of six European countries, lifetime estimated prevalence of AN, BN, BED, sub-threshold BED, and any binge eating were 0.48%, 0.51%, 1.12%, 0.72%, and 2.15%, respectively, and they were 3–8 times higher among women for all eating disorders. Age of onset for the majority of eating disorders was between 10 and 20 years of age. Comorbidity with other mental disorders was common. Only a minority of individuals with a lifetime eating disorder requested medical treatment.


In Project TR-EAT, the symptomatic status of eating-disordered patients (AN, N = 233, BN, N = 422) was tracked after inpatient treatment over a 2.5-year follow-up period. The distribution of time to relapse for both disorders and possible predictors for relapse are investigated by means of discrete time survival analysis. Fifty-eight per cent of the patients with AN and 74% of those with BN achieved partial remission before end of treatment, and thus were at risk for relapse. The relapse rates within 2.5 years were 32.6% for AN and 37.4% for BN. For both eating disorders, the highest risk of relapse was within the first 6 or 7 months after achieving partial remission.


*Neuropsychopharmacology*, 35, 147-168. [https://doi.org/10.1038/npp.2009.115](https://doi.org/10.1038/npp.2009.115)


*Swedish register data were used to identify a sample of 850 individuals diagnosed with binge-eating disorder (BED). Associations were examined between BED and neurologic, immune, respiratory, gastrointestinal, skin, musculoskeletal, genitourinary, circulatory, and endocrine system diseases. Compared with controls matched on sex, year, month, and county of birth, BED was associated with an increased risk for most classes of disease. The strongest associations were found between BED and diabetes and cardiovascular system diseases.*


*This is one of the first studies to investigate overlapping genetic and environmental risk factors for anorexia nervosa, major depression, and suicide attempts. Findings suggest that a portion of the genetic factors underlying anorexia nervosa also contribute to liability to major depression and suicide attempts in adult women. Individual-specific environmental factors, however, may not overlap but rather are trait specific.*


*Social Psychiatry and Psychiatric Epidemiology, 36*, 343-347.


Treasure, J., Stein, D., & Maguire, S. (2015). 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. 


Eighty-five parents and 55 siblings of adolescents with anorexia nervosa completed the Strengths and Difficulties Questionnaire at diagnosis. In addition, 88 parents and 46 siblings completed the Strengths and Difficulties Questionnaire after finishing treatment. Mothers and fathers reported siblings to have lower levels of conduct problems in comparison with population norms. Mothers also reported lower levels of prosocial behaviors. Siblings reported higher levels of emotional difficulties and hyperactivity in comparison with their peers.

[https://doi.org/10.1002/erv.721](https://doi.org/10.1002/erv.721)

[https://doi.org/10.1002/erv.722](https://doi.org/10.1002/erv.722)

[https://doi.org/10.1002/eat.22421](https://doi.org/10.1002/eat.22421)

Overlapping genetic and environmental risk factors for a composite measure of eating disorders (including AN, BN, BED, and purging disorder) and suicidality were examined in female twins. Results suggest that some of the genetic factors influencing vulnerability to eating disorders also influence suicidality.

[https://doi.org/10.1093/schbul/sbv074](https://doi.org/10.1093/schbul/sbv074)
Blood and temporal lobe biopsy samples were obtained from twelve epilepsy patients during neurosurgical treatment. Findings indicate that most DNA methylation markers in peripheral blood do not reliably predict brain DNA methylation status, but a subset of peripheral data may proxy methylation status of brain tissue. Restricting the analysis to these markers may identify meaningful epigenetic differences in brain disorders.


Review of medical complications associated with anorexia nervosa and bulimia nervosa and how the complications can be treated. Epidemiology and psychiatric comorbidities of eating disorders are discussed.


Eating disorder traits and body dissatisfaction are compared across three different groups of people: 200 trans people, 200 people with eating disorders, and 200 healthy controls. Results from the study are in line with previous literature; trans individuals do not score as highly on measures of body dissatisfaction as those with clinical eating disorders. However, compared with healthy controls, trans individuals report higher eating disorder symptoms. Particular attention is paid to gender differences, as trans males had similarly high scores on measures of body dissatisfaction as males with eating disorders.


The association between eating disorders and suicide attempts was examined using national register data from Sweden. Significantly elevated risks of suicide attempts were observed in individuals with any eating disorders, anorexia nervosa, and bulimia nervosa. Elevated risks of suicide attempts were also found in relatives (full-siblings, half-siblings, and cousins) of the individuals with the aforementioned eating disorders, suggesting familial liability for eating disorders and suicide attempts.


Supplementary Figure S1. Lifetime Prevalence of Eating Disorders by Sex
References for Supplementary Figure S1


Supplementary Figure S2. World map of countries with reported prevalence or cases of eating disorders (dark blue = positive report).

References for Supplementary Figure S2


Eating Disorders, 49, 975–997. https://doi.org/10.1002/eat.22596


**Supplementary Table S1. Confidence Matrix for Review**

<table>
<thead>
<tr>
<th>Level of Confidence</th>
<th>Description</th>
</tr>
</thead>
</table>
| High                | >1 systematic review and/or meta-analysis of available evidence providing support  
                    | >1 randomized controlled trial with effects in a consistent direction  
                    | When appropriate to the research question, >2 large epidemiological studies with consistent evidence from samples in >1 area of the world |
| Moderate            | Converging body of evidence, studied across multiple sites and/or outcomes |
| Low                 | Singular studies as the only supporting evidence, a body of evidence with equivocal or conflicting findings, exclusive reliance on indirect outcome measures |
| Very Low            | Expert opinion or theory only |
**Supplementary Table S2. Detailed Evidence for Confidence Ratings of Supportive Statements**

<table>
<thead>
<tr>
<th>Supportive Statements</th>
<th>Confidence Rating</th>
<th>Basis for Confidence Rating</th>
<th>Relevant Future Investigations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Truth 1: Many people with eating disorders look healthy, yet may be extremely ill.</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1 Eating disorders are associated with significant somatic, psychosocial and psychological risk.</td>
<td>High</td>
<td>Multiple systematic reviews across several outcomes, including: GI complications (Norris et al., 2016); refeeding syndrome (O’Connor &amp; Nicholls, 2013); cardiovascular complications (Sachs, Harnke, Mehler, &amp; Krantz, 2016); mortality (Arcelus, Mitchell, Wales, &amp; Nielsen, 2011); and psychological outcomes (Berkman, Lohr, &amp; Bulik, 2007; Sheehan &amp; Herman, 2015). Additional narrative reviews summarize medical complications in eating disorders, e.g. (Mehler &amp; Brown, 2015; Mehler &amp; Rylander, 2015; Westmoreland, Krantz, &amp; Mehler, 2016). (see Supplementary Tables S3 &amp; S4)</td>
<td>Case-control and longitudinal studies distinguishing specific relationships between medical and psychological comorbidities and eating disorders to identify direction of causality.</td>
</tr>
<tr>
<td>1.2 Most individuals with eating disorders do not appear emaciated.</td>
<td>High</td>
<td>Eating disorders are present across the whole BMI range and weight is only a criterion in AN. On average BMI: AN&lt;BN&lt;BED. The prevalence of AN is lower than other eating disorders. One systematic review (Lindvall Dahlgren &amp; Wisting, 2016) and one meta-analysis (Qian et al., 2013) indicate that AN is less prevalent than BN and BED. Epidemiological data from several countries indicate that lifetime prevalence of BED is higher than that of BN, which is consistent across several countries (Kessler et al., 2013), and estimates from a large community sample of adolescents indicate that risk for BN is greater in obese as compared to normal weight adolescents. (Flament et al., 2015). Also see Statement 5.4: Eating disorders occur in individuals of all shapes and sizes.</td>
<td>Meta-analyses to provide accurate estimates of incidence and lifetime prevalence of DSM-5 eating disorders. RCTs of interventions that address both disordered eating and risk for excess weight gain in vulnerable populations. Animal research, case-control, and longitudinal studies that consider the role of metabolic dysfunction in understanding eating pathology. Longitudinal research to consider potential differences in course and outcome of eating disorders based on weight status (e.g. normal weight vs. obese individuals who binge eat).</td>
</tr>
<tr>
<td>1.3 Somatic, psychosocial, and psychological manifestations and comorbidities of</td>
<td>Moderate</td>
<td>Narrative literature reviews indicate that patients with eating disorders may present to emergency departments with symptoms such as dizziness, fatigue, syncope, and seizures due to eating disorder complications (Mascolo, Trent, Colwell, &amp; Mehler, 2012), and highlights potential for misdiagnosis of problems</td>
<td>Cross-sectional investigations of providers’ abilities to detect eating disorders in pediatric, primary care, and obstetrics and gynecology settings.</td>
</tr>
</tbody>
</table>
eating disorders may be difficult to detect.

**National survey of Accreditation Council for Graduate Medical Education programs** indicates that training in eating disorders for United States resident physicians is limited (Mahr et al., 2015).

Cross-sectional studies of UK family physicians indicate that primary care physicians do not utilize national clinical practice guidelines (Currin et al., 2007), have gaps in knowledge of eating disorders (Currin, Waller, & Schmidt, 2009), and that nonclinical features of case presentations (e.g., gender) may influence diagnosis and treatment recommendations (Currin, Schmidt, & Waller, 2007).

Cross-sectional investigation of fertility specialists in Australia indicates some misconceptions about eating disorders and low rates of screening for eating disorders in practice (Rodino, Byrne, & Sanders, 2016).

See Supplementary Tables S3 & S4 for an overview of somatic, psychosocial, psychological and neurocognitive manifestations and comorbidities associated with eating disorders.

| 1.4 | Most individuals with eating disorders do not enter treatment; those that do often do so many years into the course of illness. | High | Several epidemiological studies across many countries indicate that only a minority of individuals who meet criteria for eating disorders seek treatment (Hoek & van Hoeken, 2003; Hudson, Hiripi, Pope, & Kessler, 2007; Keski-Rahkonen et al., 2009; Kessler et al., 2013; Preti et al., 2009). | Develop and disseminate methods for early detection and referral. | Cross-sectional identification of factors that relate treatment initiation across eating disorder diagnoses. | Increasing reach of available interventions. |
| 2.1 | Biological risk factors contribute to the development of eating disorders. | High | See Truth 4: Eating disorders are not choices, but serious biologically influenced illnesses. | | | |
| 2.2 | Prototypical family interaction patterns that exist premorbidly among families with eating disorders. | Moderate | While a few studies have found parental factors associated with eating disorder onset (Johnson, Cohen, Kasen, & Brook, 2002; Nicholls & Viner, 2009; Shoebridge & Gowers, 2000), reviews and position papers that summarize longitudinal, case-control, | | | 

**Truth 2: Families are not to blame, and can be the patients’ and providers’ best allies in treatment.**
<table>
<thead>
<tr>
<th>Eating disorders have not been identified.</th>
<th>and cross-sectional research on the role of family functioning in eating disorders have not identified consistent patterns of risk associated with parenting or family interaction styles (Campbell &amp; Peebles, 2014; Eisler, 2005; le Grange, Lock, Loeb, &amp; Nicholls, 2010; Strober &amp; Humphrey, 1987; Yager, 1982).</th>
<th>Recent systematic reviews call for additional longitudinal investigations (Larsen, Strandberg-Larsen, Micali, &amp; Andersen, 2015; Saltzman &amp; Liechty, 2016).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2.3</strong> Eating disorders place stress on families.</td>
<td>Moderate</td>
<td>Case-control studies indicate burden of caring for AN and highlight that parental distress may be a consequence of the disorder (Anastasiadou, Medina-Pradas, Sepulveda, &amp; Treasure, 2014; Sim et al., 2009; Treasure et al., 2001). Cross-sectional studies indicate impairments in quality of life and high burden among caregivers (Anastasiadou et al., 2014; Martin et al., 2011; Whitney et al., 2005).</td>
</tr>
<tr>
<td><strong>2.4</strong> Family-based treatments have demonstrated effectiveness for the treatment of adolescent AN.</td>
<td>High</td>
<td>Several randomized controlled trials [e.g.; (Eisler et al., 2016; Lock et al., 2010)] and one meta-analysis (Couturier, Kimber, &amp; Szatmari, 2013) support the use of FBT for adolescent AN. Recent research also indicates that FBT may be efficacious for adolescent BN (Le Grange, Lock, Agras, Bryson, &amp; Jo, 2015; Murray et al., 2015). See Supplementary Table S5 for an overview of psychological interventions in eating disorder treatment.</td>
</tr>
</tbody>
</table>

**Truth 3: An eating disorder diagnosis is a health crisis that disrupts personal and family functioning.**

| **3.1** Eating disorders have significant medical and psychological risk. | High | See Statement 1.1: Eating disorders are associated with significant somatic, psychosocial and psychological risk. | |
| **3.2** Eating disorders produce financial burden. | High | Two small, cross-sectional studies indicate high rates of economic hardship (Gatt et al., 2014) and significant financial costs (Crow et al., 2009) associated with eating disorders. A survey of the cost of mental disorders in the UK estimated costs of eating disorders at £50.6 million in 2007, with an estimated increase to £76.4 million by 2026. The majority of cost was accounted for by loss of employment (McCrone, Dhanasiri, Patel, Knapp, & Lawton-Smith, 2007). A systematic review of cost-of-illness studies and cost-effectiveness analyses in eating disorders estimated substantial | Case-control studies examining discrepancy in food and medical expenses. Studies examining the long-term financial burden of eating disorders over time. |
| 3.3 In adolescence, eating disorders may lead to functional impairment and delays in healthy development. | Moderate | Eight-year prospective investigation found that youth with eating disorders report greater functional impairment, suicidality, mental health treatment, and unhealthy BMIs compared with unaffected youth (Stice, Marti, & Rohde, 2013).

Narrative review summarizes case-control and cross-sectional research on potential delays in healthy development for adolescents and young adults with eating disorders (Stice & Bohon, 2013). | Inclusion of secondary outcomes related to healthy development in intervention trials with child and adolescent samples. |

| 3.4 In adulthood, eating disorders may interfere with intimate relationships, reproductive health, parenting, and health-related quality of life. | Moderate | A review summarizing case-control and cross-sectional studies found gynecologic problems including menstrual disturbances across all eating disorders, unplanned pregnancy, greater gestational weight gain, obstetric complications including risk for preterm birth and low birth weight infants, higher rates of miscarriage in BN and BED; poor nutrition during pregnancy, associated polycystic ovarian syndrome in those with BN and BED; and sexual dysfunction across all eating disorders (see review (Kimmel, Ferguson, Zerwas, Bulik, & Meltzer-Brody, 2016).

Studies specific to fertility have produced mixed findings (Kimmel et al., 2016), with some case-control and cross-sectional studies finding fertility issues, and others finding comparable rates of fertility and reproduction in those with and without an eating disorder history.

One case-control study indicates higher incidence of marital problems in women with BED (Whisman, Dementyeva, Baucom, & Bulik, 2012).

Systematic reviews indicate impaired health-related quality of life among individuals with eating disorders (Ágh et al., 2015; Ágh et al., 2016). | Prospective cohort studies that examine and follow outcomes secondary to eating disorder onset. Systematic review or meta-analysis of relationship and role functioning in eating disorders. |

**Truth #4: Eating disorders are not choices, but serious biologically influenced illnesses.**
<table>
<thead>
<tr>
<th>4.1</th>
<th>Disordered eating behaviors can be guided by biological processes associated with automatic (unconscious) events.</th>
<th>Moderate-High</th>
<th>One systematic review and meta-analysis identified difficulties with inhibitory control associated with bulimic-type eating disorders (Wu, Hartmann, Skunde, Herzog, &amp; Friederich, 2013). A recent theoretical model identifies eating behaviors in anorexia nervosa as habitual behaviors, similar to compulsions in OCD, supported by case-control studies on neuropsychological and neuroimaging tasks (Godier et al., 2016; Steinglass &amp; Walsh, 2016). Evidence from animal studies and human neuroimaging support some shared neurobiology in eating disorders and addiction (Kaye et al., 2013b; O’Hara, Campbell, &amp; Schmidt, 2015). A position paper reviews literature (primarily case-control studies) that identifies alterations in neurobiological pathways related to reward and self-control associated with eating disorders (Wierenga et al., 2014).</th>
<th>Development of neuropsychologically based treatment approaches. Longitudinal examination of neuropsychological outcomes during the course of illness and intervention.</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.2</td>
<td>Biologically-influenced, fundamental personality traits and cognitive styles are associated with eating disorders.</td>
<td>High</td>
<td>Several systematic reviews and meta-analyses converge on the idea that fundamental personality traits (e.g. impulsivity, perfectionism) and cognitive styles (e.g. difficulties with set shifting) are associated with eating disorders (Cassin &amp; von Ranson, 2005; Lang, Lopez, Stahl, Tchanturia, &amp; Treasure, 2014; Lopez, Tchanturia, Stahl, &amp; Treasure, 2008; Roberts, Tchanturia, Stahl, Southgate, &amp; Treasure, 2007). Recent case-control studies and narrative reviews of the literature support and extend these findings (Balodis et al., 2013; Ehrlich et al., 2015; Kaye, Wierenga, Bailer, Simmons, &amp; Bischoff-Grethe, 2013a; Klabunde, Acheson, Boutelle, Matthews, &amp; Kaye, 2013; Lavender et al., 2015; Vall &amp; Wade, 2015). Also see Supplementary Table S4 for an overview of psychological and neurocognitive traits associated with eating disorders.</td>
<td>Updated conceptualization of eating disorder etiology for patients and caregivers. Longitudinal studies examining RCTs involving treatment matching based on phenotypic psychobiological profiles. Longitudinal investigations of specific behavioral traits that occur in childhood, prior to ED onset.</td>
</tr>
<tr>
<td>4.3</td>
<td>Individuals with eating disorders may experience non-typical responses to eating and activity.</td>
<td>Moderate</td>
<td>Case-control studies find increased attention to and value of physical activity in patients with AN (Giel et al., 2013; Klein et al., 2010).</td>
<td>Systematic reviews and meta-analyses that empirically summarize altered response to food and exercise related experiences in those with eating disorders.</td>
</tr>
</tbody>
</table>
| 4.4 Eating disorders are associated with dysregulation in neurotransmitter availability and function. | Moderate | Case-control and cross-sectional studies of ill and recovered patients indicate that individuals with eating disorders have disturbances of dopamine and serotonin systems [see reviews (Kaye et al., 2005; Kaye et al., 2013a; Kaye, 2008)].

Other case-control and cross-sectional research supports the role of leptin, ghrelin, BDNF, and endocannabinoids in eating disorders [see reviews, (Monteleone & Maj, 2013; Scherma, Fattore, Castelli, Fratta, & Fadda, 2014)]. | Basic science research identifying neural circuitry associated with eating disorder risk.

Longitudinal ambulatory assessment in the general population or birth cohorts to quantify the degree of physical activity in patients and healthy controls prior to the onset of the disorder and during the course of illness. |

| 4.5 Brain structure and function differ between those with active eating disorders and unaffected individuals. | High | Systematic reviews and meta-analyses of individuals with AN indicate alterations in brain structure during illness (Seitz et al., 2014; Titova, Hjorth, Schiöth, & Brooks, 2013; Van den Eynde et al., 2012).

Neuroimaging research indicates altered brain function in individuals with eating disorders, which may predispose individuals to or arise as a result of illness [see reviews (Frank, 2013; Frank, 2015; Kaye, 2008; O’Hara et al., 2015)]. | Systematic reviews and meta-analyses of brain function in those with eating disorders.

Longitudinal investigations to distinguish temporal sequence of changes in brain function in relation to disorder onset and maintenance. |
### 4.6 Feeding and activity behavior is biologically regulated in animals.

Controlled experiments have resulted in the development of animal models of hunger (Atasoy, Betley, Su, & Sternson, 2012) and binge eating (Murray, Tulloch, Chen, & Avena, 2015), providing evidence that eating disorders have neurobiological origins.

Controlled experiments of an activity-based anorexia rodent model (Chowdhury, Chen, & Aoki, 2015) highlight increased physical activity and reduced body weight in response to restricted food access.

See Supplementary Table S7 for an overview of brain circuitry regions involved in the regulation of feeding and eating in animal models.

Additional research is needed to determine if regions identified in animal models of feeding and eating are therapeutic entry points.

### 4.7 Endocrine changes are associated with eating disorder risk.

A growing body of longitudinal research, twin studies, case-control studies, cross-sectional studies, and animal research supports the role of endocrine changes in the onset of disordered eating in females (Baker & Runfola, 2016; Baker, Girdler, & Bulik, 2012; Klump, 2013).

See Supplementary Table S3 for an overview of endocrine changes associated with eating disorders.

Longitudinal examination of eating disorder risk during the menopause transition in women.

Investigations on reproductive milestones and sex hormones and eating disorders risk in males.

Longitudinal investigations on appetite-regulating hormones.

### Truth #5: Eating disorders affect people of all genders, ages, races, ethnicities, body shapes and weights, sexual orientations, and socioeconomic statuses.

### 5.1 Eating disorders affect both males and females.

Large epidemiological studies indicate that males are affected by eating disorders, though at lower rates than females (Hudson et al., 2007; Javaras et al., 2015; Kessler et al., 2013; Preti et al., 2009; Zerwas et al., 2015). Males and females with eating disorders may have different clinical characteristics (Welch, Ghaderi, & Swenne, 2015).

Epidemiological studies in large population-based registers applying DSM5 criteria globally to assess global distribution and region-specific risk factors.

### 5.2 Eating disorders occur across the lifespan.

Large epidemiological studies indicate that eating disorder risk fluctuates with age, though eating disorders occur at all ages (Keski-Rahkonen et al., 2009; Munkholm et al., 2016; Preti et al., 2009) with binge-eating disorder being more common in older individuals (Pike, Dunne, & Addai, 2013; Smink, van Hoeken, & Hoek, 2012).

Longitudinal examination of eating disorder development during midlife and later life.
<table>
<thead>
<tr>
<th>Section</th>
<th>Description</th>
<th>Evidence</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.3</td>
<td>Eating disorders occur in all races and ethnicities.</td>
<td>High</td>
<td>A systematic review of sociodemographic correlates of eating disorders found that ethnicity was not associated with eating disorder epidemiology (Mitchison &amp; Hay, 2014). A large epidemiological study across several countries found eating disorders in all parts of the world (Kessler et al., 2013). Narrative review of epidemiological studies in specific countries likewise suggests stable or decreasing rates of eating disorders among Caucasian groups in Western Europe and North America, with increasing rates of eating pathology in other countries and among some minority groups in North America (Pike et al., 2013; Pike, Hoek, &amp; Dunne, 2014). One meta-analysis of differences in Black and White females in North America supports that differences in body dissatisfaction among these ethnic groups are decreasing (Roberts, Cash, Feingold, &amp; Johnson, 2006). RCTs establishing the efficacy of intervention for minority populations. Global epidemiological studies especially in Africa and Asia to evaluate prevalence, incidence, and mortality globally.</td>
</tr>
<tr>
<td>5.4</td>
<td>Eating disorders occur in individuals of all shapes and sizes.</td>
<td>High</td>
<td>Longitudinal studies indicate that unhealthy weight control methods and binge eating prospectively predict increases in BMI and risk for obesity over time (Field et al., 2003; Neumark-Sztainer et al., 2006; Stice, Cameron, Killen, Hayward, &amp; Taylor, 1999; Stice, Presnell, &amp; Spangler, 2002). A longitudinal investigation found that the course of individual eating disorder symptoms, including body weight, is quite variable and does not conform to initial diagnosis (Lavender et al., 2011). A cross-sectional study of adolescents found increased risk for BN in obese, compared with normal-weight, boys and girls (Flament et al., 2015). Also see Statement 1.2: Most individuals with eating disorders do not appear emaciated. Longitudinal studies that consider weight trajectory as it may relate to eating disorder symptom development using latent class analysis.</td>
</tr>
<tr>
<td>5.5</td>
<td>Eating disorders are present across different sexual orientations and gender identities.</td>
<td>Moderate</td>
<td>Cross-sectional studies indicate that gay and bisexual males may be at increased risk for eating disorders (Brown &amp; Keel, 2012b; French, Story, Remafedi, Resnick, &amp; Blum, 1996; Hadland, Austin, Goodenow, &amp; Calzo, 2014; Russell &amp; Keel, 2002). Longitudinal studies of adolescent sexual and gender identity development and eating disorder risk.</td>
</tr>
</tbody>
</table>
Some cross-sectional evidence indicates that lesbian and bisexual women have elevated eating disorder risk as compared with heterosexual women (Hadland et al., 2014; Moore & Keel, 2003).

A cross-sectional study of college students indicates that transgender individuals are at heightened risk for eating disorders compared with cisgender sexual minority and cisgender heterosexual youth (Diemer, Grant, Munn-Chernoff, Patterson, & Duncan, 2015).

Further examination of the relationship between eating disorder risk and gender identity.

| 5.6 There is no consistent association between socioeconomic status and risk for eating disorders. | Moderate | A systematic review of sociodemographic correlates of eating disorders found that socioeconomic status was not associated with eating disorder epidemiology (Mitchison & Hay, 2014). | Further longitudinal examination of the relationship between socioeconomic status and eating disorders to clarify inconsistent patterns and proposed genetic associations. |

**Truth #6: Eating disorders carry an increased risk for both suicide and medical complications.**

| 6.1 Eating disorders are associated with premature death. | High | A meta-review examined all-cause mortality in mental disorders, finding very high all-cause mortality in AN, BN, and EDNOS also evidenced elevated all-cause mortality (Chesney, Goodwin, & Fazel, 2014). A meta-analysis of mortality rates among eating disorders found significantly elevated mortality for AN, BN, and EDNOS (Arcelus et al., 2011). A meta-analysis hypothesizing inflated mortality estimates in AN re-estimated after methodological corrections and continued to find elevated all-cause mortality in AN (Keshaviah et al., 2014). | Further international studies of mortality associated with eating disorder to identify global patterns and regional differences. |

| 6.2 Risk of suicide is elevated in eating disorders. | High | Several meta-analyses find elevated suicide risk in individuals with eating disorders (Chesney et al., 2014; Keshaviah et al., 2014; Preti, Rocchi, Sisti, Camboni, & Miotto, 2011). Recent epidemiological data suggest that comorbid psychiatric conditions increase suicide risk (Pisetsky, Thornton, Lichtenstein, Pedersen, & Bulik, 2013) and that family history of an eating disorder may relate to risk of suicide (Yao et al., 2016). | Investigations exploring the mechanism underlying the association between eating disorders and suicide. |

**Truth #7: Genes and environment play important roles in the development of eating disorders.**

| 7.1 Eating disorders run in families. | Moderate-High | Family and twin studies consistently indicate that eating disorders aggregate within families. Heritability estimates range from 0.48-0.74 in AN, 0.55-0.62 in BN, and 0.39-0.45 in BED | Further examination of the relationship between eating disorder risk and gender identity. |
| 7.2 Genes play a role in eating disorder risk. | High | Evidence consistently indicates that genetics play a role in eating disorders. (Bulik et al., 2016; Culbert, Racine, & Klump, 2011; Trace et al., 2013; Yilmaz et al., 2015). The first genome-wide significant locus for AN has been discovered which is likely to represent the turning point for genomic discovery (Duncan et al., 2017). | Global efforts to increase sample size and statistical power are underway. Increase sample size in AN GWAS. Conduct BN and BED GWAS to understand role of genetics in all eating disorders. Examination of potential rare genetic variants that occur in densely affected pedigrees. |
| 7.3 Environmental factors play a role in eating disorder risk. | High | Cross-sectional and longitudinal twin studies indicate that nonshared environmental factors account for variance in eating disorder symptoms that are not accounted for by genetic effects. Cultural pressure for thinness has been identified as one specific risk factor for eating disorders, and randomized controlled trials of interventions that reduce thin-ideal internalization have led to reductions in eating disorder symptoms (Culbert, Racine, & Klump, 2015). While thin-ideal internalization may have some genetic influence, one longitudinal twin study indicates that nonshared environmental influences were most important in the etiology of thin-ideal internalization (Suisman et al., 2014). | Longitudinal studies in birth cohorts to identify risk factors of eating disorder pathology. |
| 7.4 Only a small portion of individuals exposed to environmental risk develop eating disorders. | Moderate | While exposure to some environmental risk factors, such as the sociocultural thin ideal, are pervasive, relatively few exposed individuals develop eating disorders, providing indirect evidence that environmental risk does not act alone (Culbert et al., 2015). | Longitudinal studies that examine how environmental exposure may influence eating disorder risk differentially across individuals, including gene by environment interaction. |

**Truth #8: Genes alone do not predict who will develop eating disorders.**

| 8.1 Eating disorders do not follow Mendelian transmission patterns. | Moderate | Case-control studies examining candidate genes in eating disorders have not shown consistent effects (Yilmaz et al., 2015). | Investigation of possible rare variants of strong effect. |
| 8.2 Many cases of eating disorders are sporadic, meaning there is no known family member who | Low | Family studies indicate that the relative risk for eating disorders is higher in family members of affected individuals; however, the majority of affected individuals have no reported diagnosis in affected family members (Bould et al., 2015; Steinhausen, Jakobsen, Helenius, Munk-Jørgensen, & Strober, 2015; Strober, Freeman, Lampert, Diamond, & Kaye, 2000). This literature is | Further examination of eating disorder history among relatives. |
suffers from an eating disorder.

limited in that eating disorder history among relatives may not be fully known or accurately captured.

| 8.3 Genes and environment may co-act to influence risk for eating disorders. | Low | Twin studies indicate that genetic risk for eating disorders may be activated by hormonal changes, such as puberty [see review (Baker et al., 2012)]. Longitudinal research indicates that the learned expectations about eating and thinness mediate the relationship between personality risk and eating disorder symptoms (Combs, Smith, Flory, Simmons, & Hill, 2010; Pearson & Smith, 2015). Longitudinal twin studies have found some statistical evidence of gene by environment interaction mainly stressing developmental stages as environmental moderators. Findings are currently inconsistent across studies (Culbert, Racine, & Klump, 2015). Preliminary case-control studies of methylation and expression of candidate genes indicate the possibility of epigenetic effects that relate to eating disorder affection status (Yilmaz et al., 2015). | Large population-based studies with both genotypic and phenotypic information to probe gene x environment interplay. Case-control studies to examine potential for epigenetic effects. |

| Truth #9: Full recovery from an eating disorder is possible. Early detection and intervention are important. | |

| 9.1 A substantial portion of individuals with eating disorders achieve recovery. | High | Systematic reviews and meta-analyses evaluating the longitudinal course and outcome of eating disorders in clinical samples indicate that many individuals achieve remission/recovery (Keel & Brown, 2010; Steinhausen & Weber, 2009). An 8-year longitudinal study of a community sample of adolescents found that one-year recovery rates ranged from 91%-96% (Stice, Marti, Shaw, & Jaconis, 2009). | Establishment of uniform definitions of remission, recovery, and relapse. Using these universal definitions to re-evaluate recovery rates and update prognosis estimates. |

| 9.2 Early detection and intervention may improve prognosis. | Moderate | Cross-sectional and longitudinal studies indicate that recovery is less likely as illness progresses (Keel & Brown, 2010; Pike, 1998) and that length of illness is associated with medical, neurobiological and social deteriorations that can negatively impact the course of the disorder (Treasure, Stein, & Maguire, 2015). | Develop and evaluate strategies for early detection, intervention, and relapse prevention. |

| 9.3 Effective psychological interventions for eating disorders exist. Many, but not all, patients benefit. | High | Several systematic reviews and meta-analyses support the efficacy of psychological interventions, including family-based treatment for adolescent AN (Couturier et al., 2013), cognitive behavioral treatment (Groff, 2015; Hay, 2013; Peat, Brownley, Berkman, & Bulik, 2012), including Internet-based guided self-help approaches for BN and BED (Dölemeyer, Tietjen, Kersting, | Aim for a clinician’s toolbox that includes psychological and pharmacological interventions that are effective for a range of eating disorders in diverse populations. |
9.4 Medication can be an effective treatment component for eating disorders.

<table>
<thead>
<tr>
<th></th>
<th>High for BN/BED</th>
<th>Low for AN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systematic reviews</td>
<td>Systematic reviews indicate that medication can be effective for the treatment of BED and BN (Brown &amp; Keel, 2012a; Brownley, Berkman, Sedway, Lohr, &amp; Bulik, 2007; Hay &amp; Claudino, 2012; Reas &amp; Grilo, 2008; Shapiro et al., 2007). Systematic reviews and meta-analyses have found little evidence that medications improve AN outcomes (Dold, Aigner, Klabunde, Treasure, &amp; Kasper, 2015; Lebow, Sim, Erwin, &amp; Murad, 2013). See Supplementary Table S6 for an overview of medications in eating disorder treatment.</td>
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</tbody>
</table>

Drug development and repurposing investigations to target core biological pathology of AN; studies of long-term efficacy of medication interventions for all eating disorders; study of the effectiveness of medications for eating disorders in community settings.

See Supplementary Table S5 for an overview of psychological interventions in eating disorder treatment.

AN: Anorexia nervosa; BED: Binge-eating disorder; BMI: Body mass index; BN: Bulimia nervosa; DSM-5: Diagnostic and Statistical Manual of Mental Disorders; EDNOS: Eating disorder not otherwise specified; FBT: Family based treatment; GI: Gastrointestinal; OCD: Obsessive-compulsive disorder; PET: Positron emission tomography; RCT: Randomized-controlled trial
References for Supplementary Table S2


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## Supplementary Table S3. Somatic and Psychiatric Comorbidities and Psychosocial Manifestations Associated with Eating Disorders

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Anorexia nervosa</th>
<th>Bulimia Nervosa</th>
<th>Binge-Eating Disorder</th>
<th>Source</th>
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</thead>
<tbody>
<tr>
<td><strong>Body composition</strong></td>
<td></td>
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<tr>
<td>Body fat content and distribution</td>
<td>El Ghoch, Calugi, Lamburghini, &amp; Dalle Grave, 2014; Greco, Lenzi, &amp; Migliaccio, 2016</td>
<td></td>
<td></td>
<td>SR; NR</td>
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<tr>
<td>Increased bone marrow fat</td>
<td>Donaldson &amp; Gordon, 2015; Hardouin, Rharass, &amp; Lucas, 2016; Scheller, Burr, MacDougald, &amp; Cawthorn, 2016</td>
<td></td>
<td></td>
<td>NR</td>
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<tr>
<td>Bone mineral density</td>
<td>Osteopenia, osteoporosis and fractures (Donaldson &amp; Gordon, 2015; El Ghoch et al., 2016; Greco et al., 2016; Misra, Golden, &amp; Katzman, 2016; Misra &amp; Klibanski, 2016; Robinson, Aldridge, Clark, Misra, &amp; Micali, 2016; Schorr &amp; Miller, 2017; Solmi, Veronese, Correll, et al., 2016; Thornton &amp; Gordon, 2016; Westmoreland, Krantz, &amp; Mehler, 2016)</td>
<td>Osteopenia (Robinson et al., 2016)</td>
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<td>NR; SR; MA</td>
</tr>
<tr>
<td>Increased physical activity</td>
<td>Achamrah, Coëffier, &amp; Déchelotte, 2016; Gümmer et al., 2015</td>
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<tr>
<td><strong>Brain</strong></td>
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<tr>
<td>Gray matter atrophy</td>
<td>Seitz et al., 2014; Titova, Hjorth, Schiöth, &amp; Brooks, 2013; Westmoreland et al., 2016</td>
<td></td>
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<td>SR; MA</td>
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<tr>
<td>White matter atrophy</td>
<td>Seitz et al., 2014; Titova et al., 2013;</td>
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<tr>
<td>Outcome</td>
<td>Anorexia nervosa</td>
<td>Bulimia Nervosa</td>
<td>Binge-Eating Disorder</td>
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<td></td>
<td>Westmoreland et al., 2016</td>
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<td>QR; MA</td>
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<tr>
<td><strong>Cardiovascular system</strong></td>
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<tr>
<td>Atherosclerotic vascular disease</td>
<td>Sachs, Harnke, Mehler, &amp; Krantz, 2016</td>
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<tr>
<td>Coronary heart disease</td>
<td></td>
<td></td>
<td>Olguin et al., 2016</td>
<td>SR</td>
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<tr>
<td>Autonomic dysfunction/altered heart rate variability</td>
<td>Sachs et al., 2016</td>
<td>Increased variability (Peschel et al., 2016a, 2016b)</td>
<td>Decreased variability (Mitchell, 2016; Olguin et al., 2016)</td>
<td>SR</td>
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<tr>
<td>Decreased left ventricular mass</td>
<td>Sachs et al., 2016; Spaulding-Barclay, Stern, &amp; Mehler, 2016</td>
<td></td>
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<td>NR; SR</td>
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<tr>
<td>Decreased left ventricular end-diastolic and left ventricular end-systolic dimensions</td>
<td>Spaulding-Barclay et al., 2016</td>
<td></td>
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<td>NR</td>
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<tr>
<td>Altered heart wall thicknesses</td>
<td>Spaulding-Barclay et al., 2016</td>
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<td>NR</td>
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<tr>
<td>Lower cardiac output</td>
<td></td>
<td></td>
<td>Olguin et al., 2016</td>
<td>SR</td>
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<tr>
<td>Mitral valve prolapse</td>
<td>Sachs et al., 2016; Spaulding-Barclay et al., 2016</td>
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<td>NR; SR</td>
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<tr>
<td>Myocardial fibrosis</td>
<td>Lamzabi et al., 2015; Sachs et al., 2016</td>
<td></td>
<td></td>
<td>SR; Autopsy</td>
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<tr>
<td>Cardiomyopathy</td>
<td></td>
<td>Westmoreland et al., 2016</td>
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<td>NR</td>
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<tr>
<td>Sinus bradycardia</td>
<td>Sachs et al., 2016; Spaulding-Barclay et</td>
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<td>Outcome</td>
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<tr>
<td>Blood pressure</td>
<td>Hypotension (Sachs et al., 2016; Spaulding-Barclay et al., 2016)</td>
<td>Hypertension (Mitchell, 2016)</td>
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<td>Postural orthostatic tachycardia syndrome</td>
<td>Sachs et al., 2016; Spaulding-Barclay et al., 2016</td>
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<tr>
<td>Cardiac arrhythmias</td>
<td></td>
<td>Westmoreland et al., 2016</td>
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<tr>
<td>QT dispersion</td>
<td>Sachs et al., 2016; Spaulding-Barclay et al., 2016</td>
<td>Olguin et al., 2016</td>
<td>NR; SR</td>
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<td>QT interval prolongation</td>
<td>Sachs et al., 2016; Spaulding-Barclay et al., 2016; Westmoreland et al., 2016</td>
<td>Olguin et al., 2016</td>
<td>NR; SR</td>
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<tr>
<td>Conduction delays</td>
<td>Sachs et al., 2016; Spaulding-Barclay et al., 2016</td>
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<td>SR; NR</td>
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<tr>
<td>Junctional escape rhythms</td>
<td>Sachs et al., 2016; Spaulding-Barclay et al., 2016</td>
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<td>SR; NR</td>
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<tr>
<td>Dysregulation of peripheral vasoconstriction/vasodilatation</td>
<td>Sachs et al., 2016</td>
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<tr>
<td>Acrocyanosis</td>
<td>Sachs et al., 2016</td>
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<td>Arterial vasospasm</td>
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<td><strong>Dermatology</strong></td>
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<td>Xerosis</td>
<td>Westmoreland et al., 2016</td>
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<td>Outcome</td>
<td>Anorexia nervosa</td>
<td>Bulimia Nervosa</td>
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<tr>
<td>Lanugo hair</td>
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<td>Hair thinning</td>
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<td>Perniosis</td>
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<td>Acne</td>
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<td>Carotenoderma</td>
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<td>Callus on back of hand (Russell’s sign)</td>
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<td>Mehler &amp; Rylander, 2015</td>
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<td><strong>Immunology</strong></td>
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<tr>
<td>Increased risk of infection</td>
<td>Dobner &amp; Kaser, in press</td>
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<td><strong>Hematology</strong></td>
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<tr>
<td>Anemia</td>
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<td>Thrombocytopenia</td>
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<td>Dental erosion</td>
<td>Hermont et al., 2014; Kisely, Baghaie, Laloo, &amp; Johnson, 2015</td>
<td>Hermont et al., 2014; Kisely et al., 2015; Westmoreland et al., 2016</td>
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<td>Decayed, missing and filled teeth or surfaces</td>
<td>Kisely et al., 2015</td>
<td>Kisely et al., 2015; Westmoreland et al., 2016</td>
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<td>SR; MA</td>
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<tr>
<td>Outcome</td>
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<td>Bulimia Nervosa</td>
<td>Binge-Eating Disorder</td>
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<tr>
<td>Dry mouth</td>
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<td>Kisely et al., 2015</td>
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<td><strong>Endocrinology</strong></td>
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<td>Hypogonadotropic hypogonadism with relative estrogen and androgen deficiency</td>
<td>Allaway, Southmayd, &amp; De Souza, 2016; Donaldson &amp; Gordon, 2015; Misra &amp; Klibanski, 2016; Schorr &amp; Miller, 2017; Westmoreland et al., 2016</td>
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<td>Growth hormone resistance with low insulin-like growth factors 1 (IGF-1)</td>
<td>Fazeli &amp; Klibanski, 2014; Misra &amp; Klibanski, 2016; Schorr &amp; Miller, 2017</td>
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<td>Hyperaldosteronism</td>
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<td>Westmoreland et al., 2016</td>
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<td>Hypercortisolemia</td>
<td>Donaldson &amp; Gordon, 2015; Misra &amp; Klibanski, 2016; Schorr &amp; Miller, 2017; Westmoreland et al., 2016</td>
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<td>Mitchell, 2016</td>
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<td>Thyroid function (Low T3 syndrome)</td>
<td>Donaldson &amp; Gordon, 2015; Schorr &amp; Miller, 2017</td>
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<td>Hypooxytocinemia</td>
<td>Romano, Tempesta, Micioni Di Bonaventura, &amp; Gaetani, 2015; Rutigliano et al., 2016; Schorr &amp; Miller, 2017</td>
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<td>Donaldson &amp; Gordon, 2015; Schorr &amp; Miller, 2017; Westmoreland et al., 2016</td>
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<td>Adiponectin</td>
<td>Elevated (Khalil &amp; El Hachem, 2014; Scheller et al., 2016; Schorr &amp; Miller, 2017)</td>
<td>Elevated, normal, decreased (Khalil &amp; El Hachem, 2014)</td>
<td>Decreasd (Khalil &amp; El Hachem, 2014)</td>
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<tr>
<td>Outcome</td>
<td>Anorexia nervosa</td>
<td>Bulimia Nervosa</td>
<td>Binge-Eating Disorder</td>
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<tr>
<td>Hypo- and hypervitaminosis</td>
<td>Veronese et al., 2015; Westmoreland et al., 2016</td>
<td></td>
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<td>NR; MA</td>
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<tr>
<td>Gastrointestinal peptides</td>
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<tr>
<td>Elevated peptide YY</td>
<td>Misra &amp; Klibanski, 2016; Schorr &amp; Miller, 2017</td>
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<td>Gastrointestinal symptoms</td>
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<td>Postprandial fullness</td>
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<td>Early satiety</td>
<td>Sato &amp; Fukudo, 2015; Westmoreland et al., 2016</td>
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<td>Postprandial distress syndrome</td>
<td>Sato &amp; Fukudo, 2015</td>
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**Metabolism**

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**Obstetrics and gynecology**

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**Otolaryngology (Ear, nose, and throat)**

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**Psychiatric Comorbidities and Psychosocial Manifestations**

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NR: Narrative review; SR: Systematic review; MA: Meta-analysis; LRS: Longitudinal refeeding study; RCS: Retrospective cohort study
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<td>Difficulties with set shifting</td>
<td>Van Autreve &amp; Vervaet, 2015; Wu et al., 2014</td>
<td>Wu et al., 2014</td>
<td>Wu et al., 2014</td>
<td>SR, MA</td>
</tr>
<tr>
<td>Low self-esteem</td>
<td>Jenkins, Hoste, Meyer, &amp; Blissett, 2011</td>
<td>Jenkins et al., 2011</td>
<td>Jenkins et al., 2011</td>
<td>SR</td>
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<tr>
<td>Temperament</td>
<td>Increased persistence, harm avoidance (Atiye, Miettunen, &amp; Raevuori-Helkamaa, 2015)</td>
<td>Increased persistence, novelty seeking, harm avoidance (Atiye et al., 2015)</td>
<td>Increased harm avoidance (Atiye et al., 2015)</td>
<td>MA</td>
</tr>
</tbody>
</table>

SR: Systematic review; NR: Narrative review; MA: Meta-analysis; CR: Conceptual review
References for Supplementary Table S4


nervosa: A focused narrative review of the neurological and psychophysiological literature. *Neuroscience and Biobehavioral Reviews, 52*, 131–152.
https://doi.org/10.1016/j.neubiorev.2015.02.012


https://doi.org/10.1111/jcpp.12214


https://doi.org/10.2147/PRBM.S52656

https://doi.org/10.1097/YCO.0000000000000212


https://doi.org/10.1002/eat.22302
https://doi.org/10.1097/NMD.0000000000000366


https://doi.org/10.1016/j.neubiorev.2015.11.017

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Anorexia Nervosa</th>
<th>Bulimia Nervosa</th>
<th>Binge-Eating Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tx Source</td>
<td>Tx Source</td>
<td>Tx Source</td>
</tr>
<tr>
<td>Adolescents</td>
<td><strong>FBT</strong></td>
<td>Systematic reviews &amp; meta-analyses (Couturier, Kimber, &amp; Szatmari, 2013; Lock, 2015; Watson &amp; Bulik, 2013)</td>
<td>None</td>
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<tr>
<td>Adults</td>
<td>None</td>
<td>RCTs (Eisler et al., 2000; Eisler, Simic, Russell, &amp; Dare, 2007; Lock et al., 2010; Lock, Agras, Bryson, &amp; Kraemer, 2005; Robin et al., 1999; Russell, Szmukler, Dare, &amp; Eisler, 1987)</td>
<td>RCTs (Agras, Walsh, Fairburn, Wilson, &amp; Kraemer, 2000; Chen et al., 2003; Fairburn et al., 1995; Fairburn et al., 1991; Fairburn, Jones, Peveler, Hope, &amp; O’Connor, 1993; Mitchell et al., 2011; Poulsen et al., 2014; Wonderlich et al., 2014) Reviews (Costa &amp; Melnik, 2016; Hay et al., 2009)</td>
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<tr>
<td></td>
<td><strong>CBT-I</strong></td>
<td>Systematic reviews &amp; meta-analyses (Costa &amp; Melnik, 2016; Grilo, Reas, &amp; Mitchell, 2016; Hay, Bacalchtuk, Stefano, &amp; Kashyap, 2009; Mitchell, Agras, &amp; Wonderlich, 2007; Palavras, Hay, Filho, &amp; Claudino, 2017; Shapiro et al., 2007; Wilson, Wilfley, Agras, &amp; Bryson, 2010)</td>
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<tr>
<td></td>
<td><strong>IPT</strong></td>
<td>Reviews (Costa &amp; Melnik, 2016; Hay et al., 2009)</td>
<td><strong>IPT-G</strong></td>
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<tr>
<td>Adolescents</td>
<td><strong>FT-S</strong></td>
<td>RCTs (Agras et al., 2014; Godart et al., 2012)</td>
<td>CBT</td>
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<td><strong>IO</strong></td>
<td>RCTs (Lock et al., 2010)</td>
<td>CBT-GSH</td>
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<td></td>
<td><strong>CBT-Int-GSH</strong></td>
<td>Pilot study (Tanofsky-Kraff et al., 2014)</td>
<td><strong>Pilot</strong></td>
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<td><strong>IO</strong></td>
<td>RCTs (Lock et al., 2010)</td>
<td>CBT-GSH</td>
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<tr>
<td></td>
<td><strong>Pilot</strong></td>
<td>Pilot study (Tanofsky-Kraff et al., 2014)</td>
<td><strong>IPT</strong></td>
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<tr>
<td>Age Group</td>
<td>Anorexia Nervosa</td>
<td>Bulimia Nervosa</td>
<td>Binge-Eating Disorder</td>
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<td>Tx</td>
<td>Source</td>
<td>Tx</td>
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<tr>
<td>Adolescents (cont.)</td>
<td>FBT</td>
<td>RCTs (le Grange, Crosby, Rathouz, &amp; Leventhal, 2007; le Grange, Lock, Agras, Bryson, &amp; Jo, 2015)</td>
<td>PD</td>
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<td>Adults</td>
<td>CBT-E-I</td>
<td>RCTs (Dalle Grave, Calugi, Conti, Doll, &amp; Fairburn, 2013; Zipfel et al., 2014)</td>
<td>CBT-G</td>
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<td>FPT</td>
<td>RCTs (Wild et al., 2009; Zipfel et al., 2014)</td>
<td>CBT-GSH</td>
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<td>MANTRA</td>
<td>RCTs (Schmidt et al., 2012, 2015)</td>
<td>CBT-Int</td>
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<td>SSCM</td>
<td>RCTs (Schmidt et al., 2012, 2015)</td>
<td>ICAT</td>
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<td>PP</td>
<td>RCTs (Poulsen et al., 2014)</td>
<td></td>
</tr>
<tr>
<td><strong>Experimental Treatments</strong></td>
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<td>CBT-E-I</td>
<td>Case series (Dalle Grave, Calugi, Doll, &amp; Fairburn, 2013)</td>
<td>Case series (Lock, 2005)</td>
<td>DBT</td>
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<tr>
<td>CT</td>
<td>RCTs (Lock et al., 2013) – no differences between clinical outcomes.</td>
<td>DBT</td>
<td>Pilot study (Fischer &amp; Peterson, 2015)</td>
</tr>
<tr>
<td>Adolescents</td>
<td>CRT</td>
<td>Pilot studies (Herbrich et al., 2017; van Noort, Kraus, Pfeiffer, Lehmkühl, &amp; Kappel, 2016)</td>
<td>SP-I</td>
</tr>
<tr>
<td></td>
<td>Case reports (Cwojdzinska, Markowska-Regulska, &amp; Rybakowski, 2008; Giombini, Turton, Turco, Nesbitt, &amp; Lask, 2016)</td>
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<tr>
<td>Age Group</td>
<td>Anorexia Nervosa</td>
<td>Bulimia Nervosa</td>
<td>Binge-Eating Disorder</td>
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<td></td>
<td>Tx</td>
<td>Source</td>
<td>Tx</td>
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<td>Adolescents (cont.)</td>
<td>CRT-G</td>
<td>Pilot studies (Pretorius et al., 2012; Wood, Al-Khairulla, &amp; Lask, 2011)</td>
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<tr>
<td></td>
<td>DBT</td>
<td>Case series (Salbach-Andrae et al., 2008)</td>
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</tr>
<tr>
<td></td>
<td>ACT</td>
<td>Case series (Berman, Boutelle, &amp; Crow, 2009)</td>
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<td></td>
<td>C-TX</td>
<td>Open trial (Baucom et al., 2017; Watson &amp; Bulik, 2013)</td>
<td>DBT</td>
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<td></td>
<td>CRT</td>
<td>Case report (Kirby, Fischer, Raney, Baucom, &amp; Bulik, 2016)</td>
<td>Pilot Study</td>
</tr>
<tr>
<td>Adults</td>
<td>Case reports &amp; series (Abbate-Daga, Buzzichelli, Marzola, Amianto, &amp; Fassino, 2012; Pitt, Lewis, Morgan, &amp; Woodward, 2010; Tchanturia et al., 2008; Tchanturia, Davies, &amp; Campbell, 2007)</td>
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<td>A-BBT</td>
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<td>CRT-G</td>
<td>Pilot study (Genders &amp; Tchanturia, 2010)</td>
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</tbody>
</table>


*Summary includes treatments for loss of control eating, a key symptom of binge eating found in children.

**Includes CBT-BN (Christopher G. Fairburn & Cooper, 1989; Latner & Wilson, 2000)

***Support for weight loss in patients with BED
References for Supplementary Table S5


### Supplementary Table S6. Medications for the Treatment of Eating Disorders.

<table>
<thead>
<tr>
<th></th>
<th>Anorexia Nervosa</th>
<th>Bulimia Nervosa</th>
<th>Binge-Eating Disorder</th>
<th>Source</th>
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<tr>
<td><strong>Approved</strong></td>
<td></td>
<td></td>
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<tr>
<td>None (Campbell &amp; Peebles, 2014; McElroy, Guerdjikova, Mori, &amp; Keck, 2015; Miniati et al., 2016)</td>
<td></td>
<td>Fluoxetine (only US) (McElroy et al., 2015)</td>
<td>Lisdexamfetamine (Comiran, Kessler, Fröehlich, &amp; Limberger, 2016; Grilo, Reas, &amp; Mitchell, 2016; Guerdjikova, Mori, Casuto, &amp; McElroy, 2016; Reas &amp; Grilo, 2014, 2015)</td>
<td>Narrative review, systematic review</td>
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<td></td>
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<tr>
<td><strong>Under Investigation/Published</strong></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Olanzapine (weight gain), dronabinol (weight gain), estrogen (improvement of anxiety) (McElroy et al., 2015)</td>
<td></td>
<td>Bupropion (mild weight loss), baclofen (reduction of binge-eating), chromium (improvement of glucose regulation), naloxone (reduction of time spent binge-eating) (McElroy et al., 2015)</td>
<td>Systematic review</td>
<td></td>
</tr>
</tbody>
</table>
References for Supplementary Table S6


Miniati, M., Mauri, M., Ciberti, A., Mariani, M. G., Marazziti, D., & Dell’Osso, L. (2016). Psychopharmacological options for adult patients with anorexia nervosa. *CNS Spectrums, 21*, 134–142. [https://doi.org/10.1017/S1092852914000790](https://doi.org/10.1017/S1092852914000790)


### Supplementary Table S7. Brain Circuitry Regions Involved in the Regulation of Feeding and Eating Identified Through Optogenetics and Chemogenetics.

<table>
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<tr>
<th>Brain Region</th>
<th>Nuclei involved in feeding and eating</th>
<th>Source</th>
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<tbody>
<tr>
<td>Hypothalamic nuclei</td>
<td>Arcuate nucleus</td>
<td>Aponte, Atasoy, &amp; Sternson, 2011; Betley, Cao, Ritola, &amp; Sternson, 2013; Denis et al., 2015; Kim et al., 2015; Krashes et al., 2011</td>
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<tr>
<td></td>
<td>Paraventricular nucleus</td>
<td>Aponte, Atasoy, &amp; Sternson, 2011; Betley, Cao, Ritola, &amp; Sternson, 2013; Denis et al., 2015; Kim et al., 2015; Krashes et al., 2011</td>
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<td></td>
<td>Lateral hypothalamus through the ventral tegmental area</td>
<td>Barbano, Wang, Morales, Wise, 2016; Betley et al., 2013; Broberger, Johansen, Schalling, &amp; Hökfelt, 1997; Jennings et al., 2015; Nieh et al., 2015; Nilsson et al., 2011; Nilsson, Lindfors, Schalling, Hökfelt, &amp; Johansen, 2013; Stuber &amp; Wise, 2016</td>
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<tr>
<td>Hindbrain</td>
<td>Parabrachial nucleus</td>
<td>Carter et al., 2013; Wu, Clark, &amp; Palmiter, 2012</td>
</tr>
<tr>
<td></td>
<td>Nucleus of the solitary tract</td>
<td>Wang et al., 2015; Wu et al., 2012</td>
</tr>
</tbody>
</table>
References for Supplementary Table S7

https://doi.org/10.1038/nn.2739


https://doi.org/10.1016/j.cell.2013.11.002


https://doi.org/10.1038/nn.3767


