



Impact of broadening definitions of anorexia nervosa on sample characteristics

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ABSTRACT

Practical limitations and sample size considerations often lead to broadening of diagnostic criteria for anorexia nervosa (AN) in research. The current study sought to elucidate the effects of this practice on resultant sample characteristics in terms of eating disorder behaviors, psychiatric comorbidities, temperament and personality characteristics, and heritability point estimates. Three definitions of AN were created: meeting all Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria for AN (AN-DSM-IV), meeting all DSM-IV criteria except criterion D, amenorrhea, (AN-noD), and broadening DSM-IV AN criteria by allowing a higher body mass index value, eliminating criterion D, and allowing less stringent body weight concerns (AN-Broad). Using data from the Swedish Twin Registry, 473 women fit one of the three definitions of AN. Women with AN-DSM-IV reported significantly more eating disorder behaviors than women with AN-Broad. Women with AN-noD reported more comorbid psychiatric disorders than women with AN-DSM-IV and AN-Broad. Temperament and personality characteristics did not differ across the three groups. Heritability point estimates decreased as AN definition broadened. Broadening the diagnostic criteria for AN results in an increased number of individuals available for participation in research studies. However, broader criteria for AN yield a more heterogeneous sample with regard to eating disorder symptoms and psychiatric comorbidity than a sample defined by narrower criteria.

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1. Introduction

In general, for psychiatric disorders, diagnostic criteria and criteria used for inclusion in research studies should provide a balance between validity and reliability, encompassing scientific and non-scientific components of the disorder (Kendler, 1990) and should identify a group of individuals who are fairly homogeneous and distinct from other groups (Kendell and Jablensky, 2003). Along with being able to distinguish affected from unaffected individuals accurately, diagnostic criteria need to be easily applied (First et al., 2004; Kopelman and Fleming, 2002), provide guidance in choosing an appropriate treatment likely to lead to a positive outcome (First et al., 2004), and, with advancing technology might assist with determining appropriate pharmacologic agents to treat psychiatric disorders.

With reference to anorexia nervosa (AN), criteria for inclusion in research studies should yield a group of individuals who can be easily distinguished from individuals without AN and who are similar in terms of eating disorder symptoms, psychiatric comorbidity, and personality and temperament characteristics. This would result in a homogeneous group of individuals for whom treatment could be developed, tested, and applied and yield optimum definitions of cases and controls for genetic studies. Inclusion of individuals with a precise phenotype in genetic studies could lead to improved knowledge about biological origins of the disorder and might provide potential pharmacologic targets. However, broader definitions of psychiatric disorders, which do not lose the central pathological constructs and validators of the disorder, could provide a larger group of individuals to study and might better capture individuals with similar core psychopathologies, thus preventing fragmentation of psychiatric disorders (Kendler, 1990). Although the ideal breadth of diagnostic criteria might differ depending on the purpose of the study, understanding the effect of broadening definitions of illness remains important for interpreting findings and considering generalizability.

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1.1. Arguments for relaxation of inclusion criteria in research studies

Researchers have relaxed diagnostic criteria for AN for a variety of reasons, but most commonly to boost sample size. One justification for relaxing criteria is the view that subthreshold and threshold eating disorders as lie along a continuum of severity (Keel et al., 2005; Lucas et al., 1991; Walters and Kendler, 1995) or a continuum of time as many individuals with subthreshold AN later develop threshold AN (Agras et al., 2009; Milos et al., 2005). It has been argued that women who meet diagnostic criteria for AN do not differ qualitatively from those who meet criteria for subthreshold AN (Cachelin and Maher, 1998; Crow et al., 2002; Garfinkel et al., 1996; Walters and Kendler, 1995; Watson and Andersen, 2003). In addition, the appropriateness of current measures of criterion A (low weight) (Mitchell et al., 2005) and the usefulness of criterion D (amenorrhea) have been questioned (Attia and Roberto, 2009; Gendall et al., 2006; Mitchell et al., 2005; Poyastro Pinheiro et al., 2007; Wilfley et al., 2007). Decisions to broaden diagnostic criteria usually result from a balanced consideration of the appropriateness, validity, and utility of the specific diagnostic criterion and statistical power.

However, several potential issues arise when criteria are broadened. First, studies have not uniformly relaxed diagnostic criteria rendering the comparison of results across studies difficult (Dellava et al., 2009; Dingemans et al., 2006; Dominguez et al., 2007; Haas et al., 2009; Kaye et al., 2008, 2000; Keel et al., 2005; Klump et al., 2001; Loeb et al., 2007; Perkins et al., 2005; Reba et al., 2005; Sanci et al., 2008; Schebendach et al., 2008; Wild et al., 2009). Second, women with subthreshold AN differ from women with threshold AN on eating disorder behaviors, psychiatric comorbidities, and some temperament and personality characteristics (Becker et al., 2009; Dalle Grave et al., 2008; Gendall et al., 2006; Santonastaso et al., 2009) and these differences might impact the results of research studies. Third, the extent to which genetic factors influence development of threshold and subthreshold AN might differ (Bulik et al., 2010) and inclusion of subthreshold cases could increase the number of phenocopies in the sample. If women with threshold AN differ from women with subthreshold AN, combining the groups of individuals could dilute the resulting sample, lead to

null or false findings, and potentially obscure the scientific understanding of AN.

1.2. Adjustments to criteria in research studies

Criteria for AN have generally been altered in three ways. First, criterion A, the weight criterion, has been adjusted (Bulik et al., 2010, 2009; Dellava et al., 2009; Haas et al., 2009; Kaye et al., 2008; Keel et al., 2005; Klump et al., 2001; Loeb et al., 2007; Perkins et al., 2005). Second, requirements for the number of AN criteria endorsed have varied (Dingemans et al., 2006; Keel et al., 2005; Klump et al., 2001; Perkins et al., 2005; Sanci et al., 2008; Wild et al., 2009). Third, criterion D, amenorrhea, has often been eliminated (Dominguez et al., 2007; Kaye et al., 2008, 2000; Reba et al., 2005; Schebendach et al., 2008; Wade et al., 2008).

1.3. Similarities and differences between women with threshold and subthreshold AN

Although the practice of relaxing diagnostic criteria for AN in research is common, its impact on the nature of the resultant study samples is unclear and requires further investigation. For example, eating disorder pathology has been reported to be lower in those not meeting criterion B (fear of weight gain at a low weight) (Becker et al., 2009; Thomas et al., 2009) and inconsistent in those not meeting criterion A (Santonastaso et al., 2009; Thomas et al., 2009) or criterion D (Dalle Grave et al., 2008; Gendall et al., 2006), compared with women with threshold AN. Table 1 highlights observed similarities and differences.

1.4. Diagnostic criteria and heritability

The impact of altering diagnostic criteria on heritability estimates for AN remains unknown. The risk of having AN in a cotwin of a twin affected with AN was higher when a narrow, compared with a broad, definition of AN was used (Walters and Kendler, 1995). Although heritability point estimates have exceeded 50% using several subthreshold definitions of AN (Klump et al., 2001; Kortegaard et al., 2001; Wade et al., 2000), higher heritability estimates for threshold than subthreshold AN have also been

Table 1
Similarities and differences between women who met criteria for subthreshold or threshold anorexia nervosa^a.

Study	Main findings
Santonastaso et al., 2009 Thomas et al., 2009	Excessive exercise – more likely in subthreshold (no A) than threshold Overall eating disorder pathology – similar in subthreshold (no A) and threshold Comorbid psychiatric disorders – similar in subthreshold (no A) and threshold
Becker et al., 2009; Thomas et al., 2009 Thomas et al., 2009 Cachelin and Maher, 1998 Cachelin and Maher, 1998; Dalle Grave et al., 2008; Gendall et al., 2006; Thomas et al., 2009 Thomas et al., 2009 Dalle Grave et al., 2008	Overall eating disorder pathology – lower in subthreshold (no B) than threshold Comorbid psychiatric disorders or symptoms – similar in subthreshold (no B) and threshold Body image concerns – similar in subthreshold (no D) and threshold Comorbid psychiatric disorders or symptoms – similar in subthreshold (no D) and threshold
Dalle Grave et al., 2008; Gendall et al., 2006 Dalle Grave et al., 2008 Garfinkel et al., 1996 Gendall et al., 2006	Overall eating disorder pathology – similar in subthreshold (no D) and threshold Self-induced vomiting – more likely in subthreshold (no D) than threshold Binge eating – more likely in subthreshold (no D) than threshold Excessive exercise – less likely in subthreshold (no D) than threshold Lowest body mass index – higher in subthreshold (no D) than threshold Lowest body mass index – similar in subthreshold (no D) and threshold Persistence – lower in subthreshold (no D) than threshold Smoking – higher in subthreshold (no D) than threshold
Gendall et al., 2006; Santonastaso et al., 2009 Santonastaso et al., 2009	Novelty seeking – higher in subthreshold (no D) than threshold Anxiety – more likely in subthreshold (no D) than threshold Obsessionality – more likely in subthreshold (no D) than threshold

^a Subthreshold definitions indicated by which criterion was relaxed; no A = did not meet Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criterion A (low weight); no B = did not meet DSM-IV criterion B (fear of weight gain at low weight); no D = did not meet DSM-IV criterion D (amenorrhea).

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