Behavior Genetics, Vol. 29, No. 1, 1999

A Genetic Analysis of the Eating and Attitudes Associated with Bulimia Nervosa: Dealing with the Problem of Ascertainment in Twin Studies

Tracey Wade,[1,4] Michael C. Neale,[2] Robert I. E. Lake,[3] and Nicholas G. Martin[3]

Received 11 Nov. 1997—Final 25 Nov. 1998

Little is known about the etiology of bulimia nervosa and the attitudes associated with it. We have undertaken a study of selected (45 pairs) and unselected (106 pairs) female twins to elucidate the broad causes of individual differences in these behaviours and attitudes. The selected sample was chosen on the basis of at least one of the twin pair having a lifetime incidence of bulimia nervosa. Biometrical model fitting, which corrected for the biased twin correlations of the ascertained group, was used to investigate the genetic and environmental risk factors contributing to the development of bulimia nervosa. The best-fitting model showed that individual variation was best explained by additive genetic influences (62%) and nonshared environmental influences (38%). The proportion of genetic variance affecting individual variation in the ascertained group and the random group was not found to be significantly different. In summary, it is suggested that it may not be necessary to supplement a randomly selected sample with an ascertained sample when investigating the liability to a low-prevalence psychiatric disorder if a continuous measure of that disorder is available.

KEY WORDS: Bulimia nervosa; ascertainment correction; genetic analysis; eating disorders.

INTRODUCTION

The lifetime prevalence of bulimia nervosa in females is estimated to be about 2% (Fairburn and Beglin, 1990), a low-prevalence disorder compared to other psychiatric conditions, such as anxiety (lifetime prevalence range, 3–13%) or depression (affecting 5–25% of the population) [American Psychiatric Association (APA), 1994]. A DSM-IV (APA, 1994) diagnosis of bulimia nervosa requires the presence of both an attitudinal component ("self-evaluation is unduly influenced by body shape and weight") and the behavioral components of binge eating and inappropriate methods of weight control, such as self-induced vomiting. We know that the behaviors are widely present in the Western female population, with a "normative discontent" existing with regard to weight and shape (Rodin *et al.*, 1984) and up to a third of women having used inappropriate means of weight control at some stage of their life (Wade *et al.*, 1996). While a diagnosis of bulimia nervosa is required to satisfy certain diagnostic criteria, it is also widely recognized as a heterogeneous and complex disorder, with a variety of other clinical features often being present (Fairburn, 1991; Beumont, 1988; Vitousek and Manke, 1994).

Currently there exists limited knowledge of the etiology of eating disorders and the contributing risk and protective factors (Hewitt, 1997). While a handful of clinically ascertained twin samples have been examined in an attempt to identify to what extent risk factors for bulimia nervosa are genetic or environmentally determined (Treasure and Holland, 1990; Fichter and Noegel, 1990; Hsu *et al.*, 1990), only one research

[1] Department of Psychology, Flinders University of South Australia, Australia.
[2] Department of Psychiatry, Medical College of Virginia, Richmond, Virginia 23298.
[3] Department of Epidemiology, Queensland Institute of Medical Research, Queensland, Australia.
[4] To whom correspondence should be addressed at Virginia Institute for Psychiatric and Behavioral Genetics, Virginia Commonwealth University, P.O. Box 980126, Richmond, Virginia 23298-0126. e-mail:tdwade@hsc.vcu.edu. Fax: +1 804-828-1471.

0001-8244/99/0100-0001$16.00/0 © 1999 Plenum Publishing Corporation

group has utilized a large, population-based twin registry (Kendler *et al.*, 1991, 1995; Sullivan *et al.*, 1998). To date, results indicate that the etiology of bulimia nervosa (as defined by a categorical conceptualisation of the phenotype) has moderate heritability, with some indication that the environmental influences arise from both shared and nonshared environmental experiences (Kendler *et al.*, 1991, 1995). It is suggested that there remains a need for additional twin studies involving different populations, a closer focus on the development of eating disorders, and a reconsideration of the value of dimensional versus categorical definition of the phenotype (Hewitt, 1997).

The majority of research in twin work is generally based around the collection of information from twin pairs sampled at random from the population. However, when studying low-prevalence psychiatric disorders such as bulimia nervosa, it can be more efficient, and increase the power of the analysis, to ascertain twin pairs in which at least one is affected by the disorder in question (Neale *et al.*, 1994). However, such a sample omits pairs where both are unaffected and so covariance matrices calculated from these selected samples will be biased away from their population values (Martin and Wilson, 1982; Neale *et al.*, 1989). Therefore, some adjustment for the effects of ascertainment must be made, in order to correct for the necessarily missing pairs concordant for being below the threshold or selection cutoff point. The software package Mx (Neale, 1997) can be used to correct for ascertainment.

The major purpose of this study is to present a univariate genetic analysis of a quasi-continuous measure of attitudes which predicts risk for the development of bulimia nervosa. These attitudes are thought to be instrumental in the development of bulimia nervosa (Cooper and Fairburn, 1993). The twin sample included in this study contains pairs selected from the Australian NHMRC Twin Registry (ATR) on the basis of past eating problems (*i.e.*, an ascertained sample) and others randomly selected from the same registry. An additional methodological aim is to extend and apply the methods of ascertainment correction in selected twin samples.

METHODS

Sample

Female twins (MZ and DZ same-sex pairs only) participating in the current study had been assessed previously for disturbed eating patterns in 1988 (Wave 1; N = 2805 women) and 1992 (Wave 2; N = 3144 women). Wave 1 assessment consisted of a "Health and Lifestyle" self-report questionnaire which contained five questions assessing whether the woman had ever experienced problems, or ever had treatment for, a variety of types of disordered eating. These questions did not permit the formal diagnosis of DSM diagnosis of bulimia nervosa but did indicate the likely incidence of such a disorder. Wave 2 assessment consisted of a general psychiatric telephone interview schedule, part of which assessed for lifetime prevalence of DSM-III-R bulimia nervosa (APA, 1987). For further details see Wade *et al.* (1996).

The participants in this current study were a sample of 325 women, chosen for a telephone interview, carried out during 1994 and 1995. These interviews constitute Wave 3 data, which are analyzed in this study. Zygosity was determined through the use of two standard questions, addressing whether they had been mistaken for their twin when growing up and resemblance of features to their twin. To be eligible, the women had to meet three criteria. First, at least one member of the twin pair had to have participated in either Wave 1 or Wave 2 assessment. Second, only women from female–female MZ and DZ pairs were approached, *i.e.*, females from DZ opposite-sex pairs were excluded. Third, in order to maximize the chance that any eating disorder was likely both to have already occurred and to be accurately recalled, only women aged between 30 and 45 years at Wave 1 data collection were interviewed. This age range was selected because the mean age at onset of bulimia nervosa is about 20 years (Keck *et al.*, 1990; Kendler *et al.*, 1991), with a linear increase in the number of women experiencing their first symptom between the ages of 14 and 25 (Bushnell *et al.*, 1990) and few new cases of bulimia nervosa occurring after age 25 (Woodside and Garfinkel, 1992). Two samples of twins were selected for interview: the first, a random sample of twin pairs; and the second, all twin pairs where one or both met the criteria for a possible lifetime diagnosis of bulimia nervosa on Wave 1 or Wave 2 assessment. Those who had already been selected for the random sample were deleted from the ascertained sample (N = 7 pairs).

In all, twins from 206 pairs were approached for interview and a total of 151 complete pairs and 23 incomplete pairs (one twin only) were actually interviewed (Table I). For valid ascertainment correction to apply, the same effort to contact and interview should be applied to *all* individuals in the sample, regardless of zygosity or their cotwins' cooperation status, as dif-

Table I. Pattern of Responses from Twin Pairs Approached for the EDE Interview for Both the Random Group and the Ascertained Group

	Random	Ascertained
Both twins interviewed (**MZ/DZ**)	106 (**70/36**)	45 (**24/21**)
One twin interviewed (**MZ/DZ**)	13 (**8/5**)	10 (**4/6**)
Other twin refused	*10*	*3*
Other twin not traced	*3*	*7*
Neither twin interviewed	23	9
Refusal, cotwin not approached	*18*	*8*
Twin not traced	*5*	*1*
Total pairs approached ($N = 206$)	142	64

ferences in the eating disorder rates between interview-concordant and interview-discordant pairs could be due to either the differential effort in gathering data or a volunteering effect. Our procedure does not meet the ideal requirements for complete ascertainment in that 9 women (14%) in the ascertained sample and 23 women (16%) in the random sample should have been interviewed without regard to the refused or untraceable status of the cotwin.

Assessment

Wave 3 assessment consisted of the Eating Disorder Examination (EDE) (Fairburn and Cooper, 1993), a semistructured interview that provides DSM-IV (APA, 1994) diagnoses of eating disorders. The lifetime prevalence of bulimia nervosa in the random and ascertained groups was 4 and 19, respectively. The EDE also provides a continuous measure of disordered eating and the core psychopathology associated with eating disorders existing over the month preceding interview (Cooper and Fairburn, 1993). Each item is measured on a 7-point scale of severity, and the final total on the EDE, which is the average of all items, ranges from 0, indicating no problems, to 6, indicating frequent and severe problems. A typical item is, "Over the past 4 weeks has your shape/weight been important in influencing how you feel about yourself as a person? If you imagine the things that influence how you feel about yourself—such as your performance at work, being a parent, your marriage, how you get on with other people—and put these things in order of importance, where does shape/weight fit in?" The 7-point rating scale ranges from "no importance" to "supreme importance (nothing is more important in the subject's scheme for self-evaluation)." The EDE has been described as being unmatched for its depth and breadth of the assessment of the attitudinal and behavioral characteristics that define bulimia nervosa (Wilson, 1993) and has been shown to be reliable and have acceptable discriminant validity (Rosen *et al.*, 1990; Wilson and Smith, 1989). The women in the ascertained group had significantly more disturbed attitudes than the women in the random group (Wade *et al.*, 1997a).

Administration of the EDE

The EDE is usually administered as a face-to-face interview but has also been used satisfactorily as a telephone interview. Telephone interviews of the EDE were used in this study for two reasons. First, the sample interviewed was from all over Australia, and face-to-face interviews would have been too expensive. Second, findings from the research literature suggest that the use of telephone interviews with the EDE, as opposed to face-to-face-interviews, yield similar results. Research comparing these two modes of interviewing suggests that there is a high correlation for general lifetime psychiatric diagnoses (Sobin *et al.*, 1993; Fenig *et al.*, 1993). If anything, there is some suggestion that telephone interviewing may yield better response rates and promote higher compliance rates to the completion of individual items (Fournier and Kovess, 1993).

The random and ascertained samples were combined and then one of each twin pair was randomly chosen to be interviewed first and these were interviewed in randomly selected order. The interviewer was blind to the results of the assessments from Wave 1 and Wave 2 data, thus any halo effects from talking to the cotwin were minimized. Once all these twins had been interviewed, the cotwins were also chosen for interviewing in random order.

Statistical Methods

The methods for analysis of the EDE data have been divided into four steps: (i) preparation of data such that the assumption of multivariate normality is met and any missing data are dealt with appropriately; (ii) investigation of the data for any systematic differences or biases resulting from effects of selected sampling; (iii) correction of the twin correlations for ascertainment; and (iv) parameterization of twin correlations in terms of postulated latent sources of genetic and environmental variance.

Data Preparation

Structural equation modeling depends on the assumption of multivariate normality, but the distribution of the EDE scores is strongly positively skewed (Fairburn and Cooper, 1993). The true distribution of liability to eating disorders is not known but may be normal if the Central Limit Theorem applies (*i.e.,* if there are many risk factors each of a small effect influencing the liability to eating disorders). The EDE is unable to detect fully this hypothesized continuous variation in liability and thus the Wave 3 data were transformed by assigning each category its corresponding normal weight. To this end, the distribution of the raw eating scores in the *randomly selected* group was divided into approximate deciles, and 10 normal weights were assigned to these classes, making use of the thresholds calculated by PRELIS 2.03 (Joreskog and Sorbom, 1993): these were then applied to the ascertained subsample. This same procedure was applied to the data from Waves 1 and 2, using semicontinuous raw eating scores. Further details of these transformations can be obtained from the author. Further, to make use of all the observations, and to avoid losing cases through listwise deletion, maximum-likelihood (ML) analysis of individual observations was employed using the *raw data* option in Mx (Neale, 1997).

Testing for Volunteer Bias

Investigations showed that there was no bias with regard to previous eating problems for those women who refused to do the interview compared to those who agreed (Wade *et al.,* 1997b). Typically in any study involving consent of human subjects, one expects to find a proportion of subjects refusing to participate. If sampling has been satisfactory, we would expect to find the same mean and variance in concordant-participant pairs as in discordant-participant pairs. The presence of mean or variance differences between these groups is an indication that biased sampling may have occurred with respect to the variable under investigation (Neale and Eaves, 1993). When the means and variances are constrained to be the same between concordant-participant and discordant-participant pairs for the random group, no significant differences were found [χ = 4.73, (df = 10), $p > .9$]. There were insufficient numbers to allow this calculation in the ascertained group.

Correcting for Ascertainment

We must correct for the ascertainment of the subsample at Wave 3 on the basis of their being thought to have an eating disorder from Wave 1 or 2 data. There are two possible approaches to ascertainment correction. The first minimizes the effects of ascertainment by analyzing together the full screened samples at Waves 1 and 2 with the smaller subsamples used at Wave 3 (Little and Rubin, 1987). The second approach uses a correction procedure with the Wave 3 data alone. This second approach was utilized in this present study and the ascertainment correction procedure is detailed in the Mx script in the Appendix. The commonly suggested lifetime prevalence of bulimia nervosa (Kendler *et al.,* 1991; Bushnell *et al.,* 1990) and, also, the prevalence of bulimia nervosa found in our female population participating in Wave 2 are 2%, corresponding to the standard normal deviate of 2.0537, and it is this threshold which is used for ascertainment correction. The likelihood of pairs not being in the ascertained sample, *i.e.,* when both fall below the threshold, can be expressed as a double integral of the bivariate normal distribution:

$$L_A = \int_{-\infty}^{t}\int_{-\infty}^{t} \phi(v_1, v_2)dv_2dv_1$$

where v_1 and v_2 are dummy variables for integration over the normal distribution of the liability for individuals 1 and 2, and ϕ is the bivariate normal probability density function. The likelihood of a pair of observations, x_1 and x_2, given the ascertainment scheme is thus

$$L(x_1, x_2|A) = \frac{\phi(x_1, x_2)}{1 - \int_{-\infty}^{t}\int_{-\infty}^{t} \phi(v_1, v_2)dv_2dv_1}$$

Use of twice the negative log-likelihood as a function to minimize, which is utilized in these analyses, gives the following ascertainment function:

$$\begin{aligned} -2\ln L(x_1,x_2|A) &= -2\left(\ln\left(\phi(x_1,x_2)\right) - \ln\left(1-\int_{-\infty}^{t}\int_{-\infty}^{t}\phi(v_1,v_2)dv_2dv_1\right)\right) \\ &= -2\ln\left(\phi(x_1,x_2)\right) + 2\ln\left(1-\int_{-\infty}^{t}\int_{-\infty}^{t}\phi(v_1,v_2)dv_2dv_1\right) \end{aligned}$$

Parameterization

Finally, ascertained corrected correlations calculated from the raw data may be parameterized in terms of genetic and environmental sources of variance, using standard methods (Neale and Cardon, 1992). This parameterization (see the Appendix) is carried out within the same Mx script used for ascertainment correction,

replacing the Covariance term "R" with the genetic and environmental sources of variance.

RESULTS

As an initial investigation of the data, the 6 × 6 maximum-likelihood estimate correlation matrix was produced using all available raw observations (transformed to normal weights) for eating disorder measures at Waves 1, 2, and 3 (Table II). By including the full screened samples at Waves 1 and 2 together with the smaller and combined subsamples used at Wave 3, the effects of ascertainment at Wave 3 are minimized by maximum-likelihood estimation (MLE), as described under Methods (Little and Rubin, 1987). The correlations between Wave 1 and Wave 2 are moderate, ranging from 0.44 to 0.61; the correlations between Wave 1 and Wave 3 tend to be a bit lower, ranging from 0.38 to 0.49; and the correlations between Wave 2 and Wave 3 are lower again, ranging from 0.30 to 0.40. For the Wave 3 data (combining both the ascertained and the random samples), the MZ correlation is 0.55 (95% CI: 0.40–0.66) and the DZ correlations is 0.22 (95% CI: –0.01–0.43).

In order to check the accuracy of this MLE approach to deriving the MZ and DZ correlations, we used the ascertainment correction script to constrain the correlations from the Wave 3 data to be the same in both the random and the ascertainment-corrected MZ groups and likewise in both the DZ groups. Using this method, the joint MZ correlation is estimated to be 0.62 (95% CI: 0.50–0.71) and the DZ correlation is 0.30 (95% CI: 0.06–0.48). These values are very close to the MLE values, indicating that this MLE method of ascertainment correction is valid.

Maximum-likelihood estimates of MZ and DZ correlation were obtained from the raw observations separately for the random sample and the selected sample, without and then with correction for ascertainment, using the script shown in the Appendix and summarized in Table III. Note that whereas the estimated means and variances for the random group are fairly close to their population values (0,1), for the ascertained group the means are considerably higher, as expected, although the expected effect in reducing variances is not as great as might be anticipated. The intrapair twin correlations of the ascertained and random groups are not significantly different [$\chi^2 = 1.228$, (df = 2), $p > .5$] once the correction for ascertainment has been made to the ascertained group, indicating that the ascertained group adds little information.

We next parameterized the covariance term "R" (Appendix) for MZ and DZ twins in terms of potential latent sources of variation: additive genetic affects (A); either dominant genetic effects (D) or common environment (C), since these two are actually negatively confounded; and individual-specific environment (E). Submodels were tested against each other for the three groups of data: (1) for the ascertained sample alone, (2) for the random sample alone, and (3) jointly for the ascertained and randomly selected samples together (Table IV).

The results from the fitting of the different submodels show, for the ascertained (corrected) group (ACG), that neither the AE nor the CE model differs significantly from the full ACE model ($\chi^2 = 0.556$, df = 1, $p > .3$, and $\chi^2 = 0.846$, df = 1, $p > .3$, respectively). For the AE model, 59% of the variance in liability is due to additive genetic action and the remaining 41% of the variance is accounted for by individual-specific environment. Model fitting to the randomly selected group correlations reveals a less ambiguous picture. The AE model is clearly the preferred model, being not significantly different from the ADE model ($\chi^2 = 0.530$,

Table II. Maximum-Likelihood Estimates of Correlations Between Twin 1 and Twin 2 on the Three Waves of Data[a]

	Wave 1/T1	Wave 2/T1	Wave 3/T1	Wave 1/T2	Wave 2/T2	Wave 3/T2
Wave 1/T1	**1.00**	0.61	0.41	0.43	0.31	0.34
Wave 2/T1	0.57	**1.00**	0.40	0.30	0.29	0.18
Wave 3/T1	0.49	0.40	**1.00**	0.32	0.31	0.55
Wave 1/T2	0.27	0.18	0.16	**1.00**	0.44	0.38
Wave 2/T2	0.08	0.10	0.01	0.56	**1.00**	0.31
Wave 3/T2	0.14	0.06	0.22	0.40	0.30	**1.00**

[a] MZ correlations are in the top right of the diagonal and DZ correlations are in the bottom left of the diagonal. Correlations between the pairs are underlined.

Table III. Means, Variances, and Correlations for Normalized EDE Scores in the Random Sample and the Selected Sample Before and After Correction for Ascertainment

Analysis	Mean T1	Mean T2	Variance T1	Variance T2	Correlation (95% CI)
1. No correction					
MZ ascertained	0.82	0.35	0.73	0.96	0.00 (.14;.65)
DZ ascertained	0.44	0.46	1.23	0.73	0.00 (−.06;.54)
2. With ascertainment correction					
MZ ascertained	0.82	0.35	0.73	0.96	0.00 (.30;.72)
DZ ascertained	0.44	0.46	1.23	0.73	0.00(.05;.63)
3. Random group					
MZ	−0.44	−0.03	0.81	1.00	0.65 (.50;.74)
DZ	0.04	0.09	1.01	1.13	0.22 (−.09;.46)

df = 1, $p > .3$), whereas the CE model has a significantly worse fit ($\chi^2 = 9.134$, df = 1, $p < .01$) than the ACE model. Parameter estimates of the AE model suggest that up to 63% of the variance in liability is due to additive genetic action and 37% is due to the individual-specific environment.

Finally, the results of a joint analysis of all four groups shows that the AE model is indistinguishable from the full ADE model. The CE model is significantly worse fitting ($\chi^2 = 8.751$, df = 1, $p < .01$) than the ACE model. Decomposition of the genetic variance suggests that 62% of the variance of the combined group is accounted for by additive genetic action and 38% of the variance is accounted for by individual-specific environment. The 95% confidence intervals of these parameters are summarized

Table IV. Results of Fitting Genetic and Environmental Models for Variation in EDE Scores to the Corrected Ascertained (AGC) and Random (RG) Groups, Separately and Jointly

Analysis and Model	Standardised Variance Components A	C	E	D	Overall Fit Function (−2 x Log Likelihood	df	Comparison of Supermodels to Full Model* χ^2diff df p
1. AAG only							
ACE	.32	.25	.43	–	−68.87	104	
AE	.59	–	.41	–	<u>−68.31</u>	105	$\chi^2 = 0.56$, df = 1, p > .3
CE	–	.50	.50	–	−68.02	105	$\chi^2 = 0.85$, df = 1, p > .3
E	–	–	1	–	−52.00	106	$\chi^2 = 16.87$, df = 2, p < .01
2. RG only							
ADE	.23	–	.36	.42	593.07	223	
ACE	.64	0!	.37	–	593.60	223	
AE	.64	–	.37	–	<u>593.60</u>	224	$\chi^2 = 0.53$, df = 1, p > .3
CE	–	.49	.52	–	602.20	224	$\chi^2 = 9.13$, df = 1, p < .01
E	–	–	1	–	629.51	225	$\chi^2 = 36.44$, df = 2, p < .01
3. AGC & RG groups							
ADE	.56	–	.39	.06	525.43	329	
ACE	.62	0!	.38	–	525.44	329	
AE	.62	–	.38	–	<u>525.44</u>	330	$\chi^2 = 0.02$, df = 1, p > .
CE	–	.49	.51	–	−534.20	330	$\chi^2 = 8.75$, df = 1, p < .01
E	–	–	1	–	577.51	331	$\chi^2 = 52.06$, df = 2, p < .01

* $\chi^2$and df are obtained by subtracting the fit function (df) of the full model from the fit function (df) of interest. For each group, the best fitting model is underlined

! On a lower bound.

Table V. 95% Confidence Intervals for the A and E Parameters for the Random Wave 3 (RG) and the Corrected Ascertained and Random Wave 3 Data (AGC)

Analysis	Parameters	Estimate	(95% CI)
1. RG	A	.63	.49–.73
	E	.37	.27–.51
2. AGC & RG	A	.62	.21–.71
	E	.38	.30–.50

in Table V. The addition of the corrected ascertained groups changes the value of the confidence intervals by only about 0.015, with the exception of the lower estimate of the additive genetic parameter. Testing the heterogeneity of genetic variation in the ascertained and random groups gave a χ^2 of 0.159 (df = 1, $p > .5$), showing that the proportion of additive genetic variance that affects individual variation in disordered eating is homogeneous between the random and the ascertained groups.

DISCUSSION

This study used the Eating Disorder Examination (EDE), a continuous measure of the attitudinal and behavioral components that define bulimia nervosa, to examine the individual causes of variation in disordered eating. Two groups of women were selected from two previous waves of data collection, the first wave being a self-report questionnaire and the second wave a semi-structured psychiatric interview. One group of female twin pairs was randomly selected, regardless of the presence or otherwise of disordered eating ($N = 225$ individuals), while another was selected specifically because at least one of the pair was thought to have had a history of bulimia nervosa ($N = 100$ individuals). The twin correlations of the latter group, the ascertained sample, required correction for bias.

The results of the univariate analysis of the EDE data indicate that correction for ascertainment increases the correlations between twin pairs. The corrected twin correlations, when constrained to be the same over the random and the ascertained groups, are 0.62 for the MZ twins and 0.30 for the DZ twins. An alternative method of ascertainment correction, namely, minimization of the effects of ascertainment through MLE with the two full waves used for screening Wave 3 and the Wave 3 data, suggests similar twin correlations. Analysis of the data suggests that individual variation in Wave 3 data is due to additive genetic variance (62%) and unique environmental variance (38%). We fail to find any evidence for a role of shared environment, as has been suggested in recent research utilizing more powerful multivariate genetic analyses (Kendler *et al.*, 1995), but this could well be due to the low power of our study, which makes it difficult to estimate A and C simultaneously (Martin *et al.*, 1978).

Results of the univariate analysis of the Wave 3 data indicate that there are no significant differences between either the correlations or the proportion of genetic variance affecting individual variation in behaviors and attitudes that influence disordered eating, for the random group and the clinical group. The 95% confidence intervals estimated for the genetic and environmental variance components of the random and ascertained groups combined were found to be hardly any smaller than for those of the random group alone. These results lead us to the somewhat tentative conclusion that the clinical sample adds very little in the way of extra information to our understanding of the causes of variation in the underlying liability to disordered eating. However, this could be because our selected sample is so small—only 100 individuals, which is only half the size of the random sample.

This finding is somewhat counterintuitive to the original expectation which guided the selection of women for interview with the EDE. In the initial stages of the study, it was thought that it would be most economic to study women who were likely to have suffered an eating disorder, in order to develop a more accurate understanding of the interplay between genetic and environmental influences in the development of disordered eating. However, in this study, information gained from the randomly selected women, who showed a range of attitudes toward eating and their bodies, dieting behaviors, and eating histories, but who on the whole were not classified as having had an eating disorder, proved to be as useful for delineating the causes of individual variation of disordered eating as was information from women with a history of eating problems. This finding is suggestive of support for the liability-threshold model (Falconer, 1965), which states that underlying a dichotomous trait, such as having had an eating disorder or not, is a normally distributed latent liability to illness. When investigating proportions of genetic and environmental variance contributing to disordered eating, it may be worth considering the use of a randomly selected population if a continuous measure of the psychiatric disorder is available. However, it is still of interest to study affected populations in

terms of developing a description of the behaviors and attitudes associated with disordered eating. Only in this way can we observe correlations and factors specific to people with bulimia nervosa.

The results of the analyses should be interpreted in the context of at least five potential limitations. The first is that the ascertained group was chosen from Wave 1 and 2 assessment, and therefore some women included in the ascertained group did not necessarily have a lifetime history of bulimia nervosa (Wade *et al.*, 1997a). However, to be selected, these women would have experienced some "greater than normal" disturbance in their eating, thus representing the extreme end of the liability for the spectrum of disordered eating. This is supported by the finding that the agreement between the affected status from Wave 2 and the diagnosis from Wave 3 was fair to moderate, with a κ of 0.59 (Wade *et al.*, 1997a). In addition, the higher means for the normalized EDE in the ascertained group suggests that selection is at least partly successful.

Second, the equal-environments assumption, which assumes that MZ and DZ twins share their environment to the same extent and therefore are equally correlated in their exposure to environmental events of etiologic importance, may possibly be violated for the particular trait of interest in this study. Physical similarity has been found significantly to influence twin resemblance for bulimia nervosa (Hettema *et al.*, 1995). This finding was interpreted in the light of the importance of body dissatisfaction in bulimia nervosa, and the authors suggested that caution is required in interpretation of studies involving eating disorders. Given that the measure used in this study consisted primarily of attitudinal constructs (concerns about eating, weight, and shape) rather than a diagnosis, it may be that twin similarity leads to a greater degree of contact, rather than the reverse, as has been found in the area of social attitudes (Posner *et al.*, 1996).

Third, despite converting the normal weights to minimize skewness, there was still considerable kurtosis, and the effect of this, and other distributional problems on departures from multivariate normality, may affect indices of fit and confidence interval estimates. Fourth, we were not able to achieve complete ascertainment with our selection of the women in the third wave of assessment, but once again, we do not expect that this would have substantially altered the findings in this paper. Finally, it would be desirable to increase further the size of our selected sample and thus investigate further the robustness of the finding indicating that the clinical sample added little to our understanding of the causes of variation.

This study has made some small contribution to the furthering of our knowledge about the etiology of bulimia nervosa. It would be useful to extend these findings, using a continuous measure of bulimia nervosa with a larger population, which will give sufficient power to detect any possible presence of shared environmental influences on the development of bulimia nervosa. Of further benefit would be the use of simulation studies with a randomly chosen population, using different thresholds and different sample sizes. This would aid us in determining the costs and benefits of using clinically augmented samples and also in developing guidelines for the interpretation of results from random samples. In addition, study of a younger population and comparison with an older population would be useful in determining the extent to which genetic and environmental determination changes with age.

APPENDIX: Mx SCRIPT USED TO CORRECT FOR ASCERTAINMENT

```
! script for ascertainment correction

G1: ascertained mz group
Data NInput = 2 NGroups = 8 NObservations = 28
Rectangular File = edemza.rec
Matrices
M Full 1 2
R Stan 2 2 Free
Mean M /
Covariance R /
Matrix M .02 .02[1]
Bound -.99 .99 R 1 2
Option RSiduals
End

G2: dummy group to calculate expected cell group proportions
data Ninput = 2
CTable 2 2
0 0
0 0
Matrices
T Full 2 1
R Stan 2 2  = R1
Thresholds T /
Covariance R /
Matrix T
2.0537 2.0537
Option Rsiduals
End
```

```
G3: Calculate ascertainment correction
Data Ninput = 0
Matrices
I Iden 1 1
J IZero 1 2
P Full 2 2  = %P2
T Full 1 1
Compute T*\ln(I–J*P*J')/
Matrix T 56
Options User-defined rsiduals multiple
End

G4: ascertained dz group
data Ninput = 2 NObservations = 27
Rectangular File = ededza.rec
Matrices
M Full 1 2
R Stand 2 2 Free
Mean M /
Covariance R /
Matrix M .02.02
Bound –.99 .99 R 1 2
Option RSiduals
End

G5: dummy group
data Ninput = 2
CTable 2 2
0 0
0 0
Matrices
T Full 2 1
R Stan 2 2  = R4
Thresholds T /
Covariance R /
Matrix T
2.0537 2.0537
Options Residuals
End

G6:calculate correction
Data Ninput = 0
Matrices
I Iden 1 1
J IZero 1 2
P Full 2 2  = %P5
T Full 1 1
Compute T*\ln(I–J*P*J')/
Matrix T 54
Options User-defined rsiduals Multiple
End

G7: Random mz group
Data Ninput = 2 Nobservations = 78
Rectangular File = edemzr.rec
Matrices
M Full 1 2
R Stand 2 2 Free
Mean M /
Covariance R /
Matrix M .02.02
Bound –.99 .99 R 1 2
Option RSiduals
End

G8: dz random group
data Ninput = 2 NObservations = 41
Rectangular File = ededzr.rec
Matrices
M Full 1 2
R Stand 2 2 Free
Mean M /
Covariance R /
Matrix M .02 .02
Bound –.99 .99 R 1 2
Option RSiduals
End
```

[1] All means are fixed at 0.02, the mean EDE score for the random group.

ACKNOWLEDGMENTS

This work was supported by grants from the National Health and Medical Research Council (Australia) to N.G.M. and the National Institute of Alcoholism and Alcohol Abuse (AA 07535; U.S.A.) to Andrew C. Heath and N.G.M. and by a Flinders URB grant to T.W. We thank Suzanne Abraham for allowing us to use her questions from the Wave 1 assessment and Andrew Heath for his advice on ascertainment. We also thank Susan Treloar for her coordination of the first-wave questionnaires and Dixie Statham for her coordination of the second-wave interviews. We particularly thank the twins for their cooperation in this research.

REFERENCES

American Psychiatric Association (1987). *Diagnostic and Statistical Manual of Mental Disorders, 3rd ed. rev.*, APA, Washington, DC.
American Psychiatric Association (1994). *Diagnostic and Statistical Manual of Mental Disorders, 4th ed.*, APA, Washington, DC.

Beumont, P. J. V. (1988). Bulimia: Is it an illness entity? *Int. J. Eat. Disord.* **7**:167–176.

Bushnell, J. A., Wells, E. A., Hornblow, A. R., Oakley-Browne, M. A., and Joyce, P. (1990). Prevalence of three bulimia syndromes in the general population. *Psychol. Med.* **20**:671–680.

Cooper, P. J., and Fairburn, C. G. (1993). Confusion over the core psychopathology of bulimia nervosa. *Int. J. Eat. Disord.* **13**:385–389.

Fairburn, C. G. (1991). The heterogeneity of bulimia nervosa and its implications for treatment. *J. Psychosom. Res.* **35 (Suppl. 1)**:3–9.

Fairburn, C. G., and Beglin, S. J. (1990). Studies of the epidemiology bulimia nervosa. *Am. J. Psychiatry* **147**:401–408.

Fairburn, C. G., and Cooper, Z. (1993). The Eating Disorder Examination. In Fairburn, C. G., and Wilson, G. T. (eds.), *Binge Eating: Nature, Assessment and Treatment,* Guilford Press, New York.

Falconer, D. S. (1965). The inheritance of liability to certain diseases, estimated from the incidence among relatives. *Ann. Hum. Genet.* **29**:51–76.

Fenig, S., Levav, I., Kohn, R., and Yelin, N. (1993). Telelphone vs face-to-face interviewing in a community psychiatric survey. *Am. J. Public Health* **83**:896–898.

Fichter, M. M., and Noegel, R. (1990). Concordance for bulimia nervosa in twins. *Int. J. Eat. Disord.* **9**:255–263.

Fournier, L., and Kovess, V. (1993). A comparison of mail and telephone interview strategies for mental health surveys. *Can. J. Psychiatry* **166**:462–471.

Hettema, J. M., Neale, M. C., and Kendler, K. S. (1995). Physical similarity and the equal-environment assumption in twin studies of psychiatric disorders. *Behav. Genet.* **25**:327–335.

Hewitt, J. K. (1997). Behavior genetics and eating disorders. *Psychopharmocol. Bull.* **33**:355–358.

Hsu, L. K. G., Chester, B. E., and Santhouse, R. (1990). Bulimia nervosa in eleven sets of twins: A clinical report. *Int. J. Eat. Disord.* **9**:275–282.

Joreskog, K. G., and Sorbom, D. (1993). *Lisrel 8: Structural Equation Modeling with the SIMPLIS Command Language,* Scientific Software International, Chicago.

Keck, P. E., Pope, H. G., Hudson, J. I., McElroy, S. L., Yurgelun-Todd, D., and Hundert, E. M. (1990). A controlled study of phenomenology and family history in outpatients with bulimia nervosa. *Comp. Psychiatry* **31**:275–283.

Kendler, K. S., MacLean, C., Neale, M. C., Kessler, K., Health, A. C., and Eaves, L. (1991). The genetic epidemiology of bulimia nervosa. *Am. J. Psychiatry* **148**:1627–1637.

Kendler, K. S., Walters, E. E., Neale, M. C., Kessler, R. C., Health, A. C., and Eaves, L. J. (1995). The structure of genetic and environmental risk factors for six major psychiatric disorders in women. *Arch. Gen. Psychiatry* **52**:374–383.

Little, R. J. A., and Rubin, D. B. (1987). *Statistical Analysis with Missing Data,* John Wiley & Sons, New York.

Martin, N. G., and Wilson, S. R. (1982). Bias in the estimation of heritability from truncated samples of twins. *Behav. Genet.* **12**:467–472.

Martin, N. G., Eaves, L. J., Kearzey, M. J., and Davies, P. (1978). The power of the classical twin study. *Heredity* **40**:97–116.

Neale, M. C. (1997). *Mx: Statistical Modeling,* Department of Psychiatry, Box 710 MCV, Richmond, VA 23298.

Neale, M. C., and Cardon, L. R. (1992). *Methodology for Genetic Studies of Twins and Families,* Kluwer Academic, Dordrecht.

Neale, M. C., and Eaves, L. J. (1993). Estimating and controlling for the effects of volunteer bias with pairs of relatives. *Behav. Genet.* **24**:239–258.

Neale, M. C., Eaves, L. J., Kendler, K. S., and Hewitt, J. K. (1989). Bias in correlations from selected samples of relatives: The effects of soft selection. *Behav. Genet.* **19**:163–169.

Neale, M. C., Eaves, L. J., and Kendler, K. S. (1994). The power of the classical twin study to resolve variation in threshold traits. *Behav. Genet.* **24**:239–258.

Posner, S. F., Baler, L. A., Heath, A. C., and Martin, N. G. (1996). Social contact, social attitudes and twin similarity. *Behav. Genet.* **26**:123–133.

Rodin, J., Silberstein, L., and Striegel-Moore, R. (1984). Women and weight. A normative discontent. In *Psychology and Gender,* University of Nebraska Press, Lincoln.

Rosen, J. C., Vara, L., Wendt, S., and Leitenberg, H. (1990). Validity studies of the Eating Disorder Examination. *Int. J. Eat. Disord.* **9**:519–528.

Sobin, C., Weissman, M.M., Goldstein, R. B., and Adams, P. (1993). Diagnostic interviewing for family studies: Comparing telephone and face-to-face methods for the diagnosis of lifetime psychiatric disorders. *Psychiatr. Genet.* **3**:227–233.

Sullivan, P. F., Bulik, C. M., and Kendler, K. S. (1998). The genetic epidemiology of binging and vomiting. *Br. J. Psychiatry* **173**:75–79.

Treasure, J., and Holland, A. (1990). Genes and the aetiology of eating disorders. In McGuffin, P., and Murray, R. (eds.), *The New Genetics of Mental Illness,* Butterworth–Heinemann, Oxford, pp. 198–211.

Vitousek, K., and Manke, F. (1994). Personality variables and disorders in anorexia nervosa and bulimia nervosa. *J. Abnorm. Psychol.* **103**:137–147.

Wade, T., Heath, A. C., Abraham, S., Treloar, A. S., Martin, N., and Tiggemann, M. (1996). Assessing the prevalence of disordered eating in an Australian twin population. *Austral. N. Z. J. Psychiatry* **30**:845–851.

Wade, T., Tiggemann, M., Martin, N., and Heath, A. (1997a). A comparison of the Eating Disorder Examination and a general psychiatric schedule. *Austral. N. Z. J. Psychiatry* **31**: 852–857.

Wade, T., Tiggemann, M., Martin, N., and Heath, A. (1997b). Characteristics of interview refusers: Women who decline to participate in interviews relating to eating. *Int. J. Eat. Disord.* **22**:95–99.

Wilson, G. T. (1993). Assessment of binge eating. In Fairburn, C. G., and Wilson, G. T. (eds.), *Binge Eating: Nature, Assessment and Treatment,* Guilford Press, New York.

Wilson, G. T., and Smith, D. (1989). Assessment of bulimia nervosa and the evaluation of the Eating Disorder Examination (EDE). *Int. J. Eat. Disord.* **8**:173–180.

Woodside, D. B., and Garfinkel, P. E. (1992). Age of onset in eating disorders. *Int. J. Eat. Disord.* **12**:31–36.

Edited by Dorret Boomsma