Original Contribution

A Method for Using Incomplete Triads to Test Maternally Mediated Genetic Effects and Parent-of-Origin Effects in Relation to a Quantitative Trait

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The authors recently developed a semiparametric family-based test for linkage and association between markers and quantitative traits. This quantitative polytomous logistic regression test allows for analysis of families with incomplete information on parental genotype. In addition, it is not necessary to assume normality of the quantitative trait. Previous simulations have shown that the new test is as powerful as the other widely used tests for linkage disequilibrium in relation to a quantitative trait. Here the authors propose an extension to quantitative polytomous logistic regression that allows testing for maternally mediated effects and parent-of-origin effects in the same framework. Missing data on parental genotype are accommodated through an expectation-maximization algorithm approach. Simulations show robustness of the new tests and good power for detecting effects in the presence or absence of offspring effects. Methods are illustrated with birth weight and gestational length, two quantitative outcomes for which data were collected in a Montreal, Canada, study of intrauterine growth restriction between May 1998 and June 2000.

association; cytochrome P-450 enzyme system; epidemiologic methods; genomic imprinting; linkage (genetics); logistic models; polymorphism, single nucleotide

Abbreviation: CYP, cytochrome P-450.

Family-based tests of linkage and association between markers and quantitative traits are popular in part because the tests are valid in the presence of genetic stratification, whereas straightforward case-control designs do not allow valid testing with admixed populations. Some tests accommodate data from incomplete nuclear families. Some methods, such as the quantitative transmission disequilibrium test and the Family Genotype Analysis Program, assume that the trait has, or has been transformed to have, a normal distribution (1, 2). Other methods, such as the family-based association test, are nonparametric and rely on covariance between a function of the trait and the genotype (3). For our methods, we consider a design in which a diallelic gene is studied in triads consisting of individuals and their parents and a quantitative trait is measured in the offspring. In a previous paper (4), we proposed a semiparametric test, using a polytomous logistic regression and expectation-maximization algorithm approach, which allows for traits that are not normally distributed and accommodates families with missing data on parental genotypes.

In addition to testing for effects of the inherited allele indicating linkage and association between a trait and a marker, researchers may also be interested in testing maternal effects, which can influence the offspring through the intrauterine environment, or parent-of-origin effects, in which an inherited allele can influence the offspring differently depending on whether it was maternal or paternal in origin. The latter occurs in species with placentas through an epigenetic mechanism called “imprinting” (5).
Previously, mixture models have been suggested which allow testing of offspring effects, maternal effects, and parent-of-origin effects with triad data (6). The mixture model approach allows for missing data on parental genotypes, but specialized software is required. Other methods in the literature include a variance components approach for assessing parent-of-origin effects, a method which requires knowing which copies of the alleles are inherited from the same parental chromosomes (or “identity-by-descent” genotype information) among siblings (7). In addition, a simple linear model approach has been suggested, which does not allow for missing data on parental genotypes (8). Neither the family-based association test nor the quantitative transmission disequilibrium test allows for maternal effects or parent-of-origin effects.

With genotyped triads, we show in this paper how both phenomena can be tested within the polytomous logistic regression framework previously described (4). The proposed approach allows for missing parental data and does not require sibling pairs, although information from multiple offspring can be incorporated, as we demonstrated in another paper (9). When including multiple siblings, dependence among siblings is accounted for by using weighted score functions. These tests extend the log-linear model for qualitative traits (10–12). Simulations are used to assess their robustness and power. We illustrate these methods by testing for effects of a cytochrome P-450 (CYP) variant allele on robustness and power. We illustrate these methods by testing for effects of a cytochrome P-450 (CYP) variant allele on birth weight and gestational length.

### MATERIALS AND METHODS

#### Proposed complete-data approach

Suppose we have triad genotype data for a diallelic (or dichotomized) marker and quantitative trait data for the offspring. Let $C$ equal 0, 1, or 2 depending on the number of copies of the variant allele the child carries, with $M$ and $F$ being similarly defined for the mother and father. The choice of which allele to designate as the “variant” turns out not to have any effect on the inference. Let $X$ denote the quantitative trait value for the offspring. The unordered parental genotypes define six mating types, denoted as $MT = \{00, 01, 02, 11, 12, 22\}$.

Our previously proposed method modeled the offspring’s genotype as a function of the quantitative trait, conditioning on parental genetic mating type (4). The idea was that if the genetic marker under study does not influence the trait and is not in linkage with any gene that does, its transmission from parents to children should be random and not related to the child’s trait value. In the previously proposed quantitative polytomous logistic regression method, a likelihood was based on a model for $Pr[C = c \mid MT = mt, X = x]$ (4). Under the null hypothesis, this model will have zero coefficients for $x$, providing a simple test using standard software.

When maternal effects or parent-of-origin effects are of interest, a straightforward extension to the above model can be written. The null hypothesis for maternal effects is that for a given pair of parental genotypes, the question of which one is maternal and which one is paternal is unrelated to the quantitative trait in the offspring. The null hypothesis for parent-of-origin effects is that the value of the quantitative trait in a heterozygous offspring is unrelated to whether the variant copy came from the mother or the father, conditional on the unordered parental genotypes. We will not need to assume mating symmetry in the population at large; for example, the proportion of parent couples with $F = 1, M = 0$ need not equal that with $F = 0, M = 1$. The extension relies on a factorization, such that

$$Pr[M, C \mid MT, X] = Pr[C \mid MT, X] \times Pr[M \mid MT, X, C]. \quad (1)$$

The test of offspring effects and the test of maternal or parent-of-origin effects can be considered independently because the above likelihood factors. The first factor in equation 1 can be modeled using the original quantitative polytomous logistic regression model. The model for the second factor, which depends on maternally mediated effects and parent-of-origin effects, is developed below.

A logistic regression model is based on informative families, in which the mother’s and father’s genotypes differ—that is, on three mating types, $MT = \{01, 02, 12\}$. We model the probability that the mother has more copies than the father for each mating type. Omitting parent-of-origin effects, the conditional probabilities that $(M > F)$ are independent of $C$ and can be written

$$Pr[M = 1 \mid MT = 01, X = x] = \exp(\delta_{01}x + \mu_{01})/[1 + \exp(\delta_{01}x + \mu_{01})]; \quad (2)$$

$$Pr[M = 2 \mid MT = 02, X = x] = \exp(\delta_{12}x + \mu_{12})/[1 + \exp(\delta_{12}x + \mu_{12})]; \quad (3)$$

$$Pr[M = 2 \mid MT = 02, X = x] = \exp((\delta_{01} + \delta_{12})x + \mu_{02})/[1 + \exp((\delta_{01} + \delta_{12})x + \mu_{02}). \quad (4)$$

For this model, which assumes that there are no parent-of-origin effects, two parameters are of interest, $\delta_{01}$ and $\delta_{12}$. We restrict the parameters, such that $\delta_{02} = \delta_{01} + \delta_{12}$, imposing the simplifying assumption that the shift in the offspring’s $X$ value for a mother with two copies of the variant allele versus zero copies would be the sum of the hypothetical shift associated with one copy versus zero copies plus the shift associated with two copies versus one copy.

The parameter $\delta_{01}(\delta_{12})$ allows the quantitative trait to be systematically higher or lower if the mother has one copy (two copies) of the variant allele relative to a mother with zero copies (one copy). $\delta_{01}$ can also be interpreted as the change in the log odds of the mother’s having one copy of the variant as opposed to zero copies for every one-unit increase in the trait; a similar interpretation applies to $\delta_{12}$. The intercepts $\mu_{mt}$ are nuisance parameters that allow for mating asymmetries unrelated to the trait under study.

If parent-of-origin effects are also of interest, a binary variable is used to indicate whether the offspring inherited only one copy of the variant allele—denoted, for example, by $I_c = 1$. This indicator is multiplied by the trait and included in the model, thereby allowing the trait coefficient to be different for a child with a single maternal copy. This works because when the child has one copy and $M > F$, that
TABLE 1. Probabilities from the polytomous logistic regression model of maternal effects and parent-of-origin effects

| Parents (MT) | Offspring (C) | Logit(Pr(M > F | MT, X, C)) |
|--------------|--------------|-----------------------------|
| 02           | 1            | $\delta_{01} + \delta_{12}X + \gamma_1X + \mu_{02}$ |
| 01           | 0            | $\delta_{01} + \mu_{01}$    |
| 12           | 1            | $\delta_{01} + \gamma_1X + \mu_{01}$ |
|              | 2            | $\delta_{12}X + \gamma_1X + \mu_{12}$ |

one copy has to have come from the mother. For example, within the $MT = 01$ mating type, the new probability that $(M > F)$ can be written

$$\Pr[M = 1 | MT = 01, X = x, C = c] = \frac{\exp(\delta_{01}x + \gamma_1X(c = 1) + \mu_{01})}{1 + \exp(\delta_{01}x + \gamma_1X(c = 1) + \mu_{01})}. \quad (5)$$

Table 1 shows the logits of the conditional probabilities for the model of both maternal and parent-of-origin effects. Here the parameter $\lambda_1$ can be interpreted as the change in the log odds that a heterozygous child inherited a maternal copy of the variant instead of a paternal copy for every one-unit increase in the trait value.

Following the models described above, when there are no maternal effects between the marker and the quantitative trait, the two parameters $\delta_{01}$ and $\delta_{12}$ are both zero. Intuitively, we exploit the fact that under the null hypothesis, the relative likelihood that the mother has more copies than the father should not be correlated with the quantitative trait in the offspring (13). Under this null hypothesis, the likelihood ratio test statistic is distributed approximately chi-squared with 2 df. For the test of no parent-of-origin effects, a 1-df likelihood ratio test of $\gamma_1 = 0$ is constructed.

In the following section, we extend the model to allow for missing data on parental genotype. A complete model for $Pr(MFC = mfc | X = x)$ makes use of the model for offspring effects augmented by a marginal model for parental mating type, as described in our previous paper (4). In addition, because we include unconstrained intercepts for each mating type and marginally model the mating type as a function of $x$, no Hardy-Weinberg equilibrium, random mating, or even Mendelian assumptions are necessary to ensure the validity of this method.

**Proposed missing-data approach**

For simplicity, we consider missing paternal genotype information, but the same approach works for missing data on maternal genotypes. The missing genotypes are assumed to be missing “at random” in Little and Rubin’s (14) sense, but we do not need to assume that rates of missing genotype data are the same for mothers and fathers. Here we use an expectation-maximization algorithm described by Dempster et al. (15). The missing-at-random assumption says that missingness does not depend on the unknown parental genotype, conditional on the observed data for the family. A complete model for $Pr(MFC = mfc | X = x) = p_{mfc}(x)$, the probability that $M = m$, $F = f$, and $C = c$ given $X = x$ for the offspring, is written using straightforward conditional probability algebra:

$$p_{mfc}(x) = \Pr[m | mt, c, x] \Pr[c | mt, x] \Pr[mt | x]. \quad (6)$$

The first factor is modeled using our logistic regression maternal effects model for $Pr(M > F)$. The second and third factors are from models proposed earlier (see our previous paper (4) for detailed descriptions). The model of $Pr[c | mt, x]$ is a polytomous logistic regression model that allows testing for linkage and association between the offspring’s trait of interest and the offspring’s genetic marker, while the model of $Pr[mt | x]$ specifies a marginal model for the parental mating type as a function of the offspring’s $x$. This marginal model for the parents provides full flexibility: We need not assume that Hardy-Weinberg equilibrium governs the mating type distributions or that the distribution of the quantitative trait does not vary across subpopulations.

Again, if there are no missing data for parents, the logarithm of the corresponding complete-data likelihood is

$$\log(L) = \sum_{i, mfc} \log(\Pr(mfc | x_i)). \quad (7)$$

For families in which only one parent and one offspring have been genotyped, their contribution to the likelihood is the sum of the probabilities from the multinomial cells corresponding to the possible $M$, $F$, and $C$. For example, suppose $M$ and $C$ are 0 and 1. Then $F$ is either 1 or 2, but not 0. This means that the contribution of this family to the observed-data log-likelihood is

$$\log(\Pr(M = 0, C = 1, F = 1 | X = x_1) + \Pr(M = 0, C = 1, F = 2 | X = x_1)). \quad (8)$$

Generalizing this, with missing data, the logarithm of the observed-data likelihood is

$$\log(L) = \sum_{\text{triads } i \text{ that are complete}} \log(\Pr(mfc | x_i))$$

$$+ \sum_{\text{triads } j \text{ that are incomplete}} \log\left(\sum_{m, f, c \text{ compatible with observed genotypes for incomplete trial } j} \Pr(mfc | x_j)\right). \quad (9)$$

The observed-data likelihood in equation 9 is maximized over choices of model parameters using the expectation-maximization algorithm (15). The approach involves estimating the data in the expectation step and then maximizing the complete-data likelihood (equation 7) in the maximization step. The theory guarantees that the likelihood for the observed data, as in equation 9, will increase with each iteration of the expectation-maximization algorithm, and convergence will be achieved if a unique maximum exists.

As shown in our previous paper (4), the probabilities that triads with missing data fall into each of the possible $MFC$ categories are estimated in the expectation step. Consider the family described above. The conditional probability that the missing father has one copy of the variant allele is equal to...
Simulation methods

We generated simulations of 1,000 studies of parent and offspring triads with offspring quantitative trait $x_i$. The simulated samples each consisted of either 300 or 500 triads, but not all triads were informative when testing for maternal effects or a parent-of-origin effect. Note that with diallelic markers, testing results are the same regardless of which parent is considered the variant allele. We mixed two subpopulations, where the exact shift depended on the number of copies of the variant allele in the admixed population. A maternally mediated effect of the marker was simulated by imposing a shift, $\lambda$, on the offspring $x$ values across both subpopulations, where the exact shift depended on the number of alleles in the mother. For tests of maternal effects, the true effect corresponded to shifts in the mean quantitative trait value equal to $\lambda/2$ for $M = 1$ and $\lambda$ for $M = 2$. Two scenarios were generated, with and without offspring effects in addition to maternal effects. When allowing additional offspring effects, the true mean was also shifted by $-0.5$ for $C = 0$ and by 0.5 for $C = 2$ in comparison with the referent $C = 1$. For tests of parent-of-origin effects, in a third scenario the only effect corresponded to a shift in the mean quantitative trait value.

RESULTS

For all of the scenarios described above, the 2-df likelihood ratio maternal effects test and the 1-df parent-of-origin effects test demonstrated a nearly nominal empirical type I error at $\alpha = 0.05$ for sample sizes of 300 and 500 families. (See the intercepts in figures 1–3.) The standard errors of the empirical type I error rate are all approximately 0.007.
of the allele and by 0.5 for offspring with two copies of the allele.

Cary, North Carolina). Data follow an additive genotypic effect, meaning that the mean quantitative trait value is shifted by \( \lambda/2 \) for offspring whose mothers have one copy of the variant allele and by \( \lambda \) for offspring whose mothers have two copies of the allele. Here underlying offspring effects were added, such that the mean quantitative trait value was also shifted by \( -0.5 \) for offspring with zero copies of the allele and by 0.5 for offspring with two copies of the allele.

(for 0.05) when 1,000 data sets are generated. For the maternal effects test, only approximately 234 families out of the 500 (140 out of 300) were informing the model, whereas for the parent-of-origin effects test, only approximately 134 (80 out of 300) families were informing the model. Type I error rates for nominal levels of 0.01 and 0.10 were also consistent with the nominal type I error (data not shown) for all three scenarios, both with complete data and with incomplete data.

All tests of maternal effects demonstrated good power, and the expectation-maximization algorithm approach with 25 percent of fathers missing data performed with almost as much power as the approach for no missing paternal data (figures 1 and 2). Under the two scenarios with and without additional offspring effects, the test of maternal effects performed nearly identically (figures 1 and 2). The test for parent-of-origin effects was less powerful than the test for maternal effects, because fewer families were informing the model (figure 3). As was found for the maternal effects model, the missing data approach with a parent-of-origin effect was only slightly less powerful than the approach with no missing data (figure 3).

APPLICATION

Polymorphisms in the gene involved with the production of CYP proteins, \( CYP1A1 \), have been shown to influence the activation of polycyclic aromatic hydrocarbons. A family-based design was used to study offspring effects, maternal effects, and gene-by-environment interactions using single nucleotide polymorphisms in the \( CYP1A1 \) gene, together with several other candidate genes (16, 17).

For a study of intrauterine growth restriction conducted at Centre Hospitalier Universitaire Mère-Enfant de l'Hôpital Sainte-Justine in Montreal, Canada, between May 1998 and June 2000, case-parent triads were sampled from families with newborns weighing less than the 10th percentile according to gestational age and sex. A sample of unaffected control families was also selected in order to test for transmission distortion in the overall population, which may exist if transmissions of the gene are not Mendelian due to allele-related selective survival. Controls were matched to the cases on the basis of gestational week, sex, and race. In total, 965 case triads and control triads were genotyped for the \( CYP1A1 \) variants. The log-linear model was used to estimate relative risks associated with specific alleles for the 493 case-parent triads (12).

For three variants considered in the \( CYP1A1 \) gene, the only statistically significant effects reported were for an offspring \( CYP1A1*2A \) variant (17). A decreased risk of intrauterine growth restriction was associated with offspring having one copy of the \( CYP1A1*2A \) variant. A relative risk of 0.73 (95 percent confidence interval: 0.51, 1.05) associated with one copy and a relative risk of 2.24 (95 percent confidence interval: 0.77, 6.45) associated with two copies were reported (17). A 2-df likelihood ratio test of

![FIGURE 2. Simulation-based estimated power of a test of maternal effects in the presence of offspring effects. A smooth line was fitted to the data using a spline routine from SAS/GRAPH (SAS Institute, Inc, Cary, North Carolina). Data follow an additive genotypic effect, meaning that the mean quantitative trait value is shifted by \( \lambda/2 \) for offspring whose mothers have one copy of the variant allele and by \( \lambda \) for offspring whose mothers have two copies of the allele. Here underlying offspring effects were added, such that the mean quantitative trait value was also shifted by \( -0.5 \) for offspring with zero copies of the allele and by 0.5 for offspring with two copies of the allele.](image1)

![FIGURE 3. Simulation-based estimated power of a test of parent-of-origin effects. A smooth line was fitted to the data using a spline routine from SAS/GRAPH (SAS Institute, Inc, Cary, North Carolina). Data were generated by shifting the mean quantitative trait value by \( \lambda \) for offspring who inherited a maternal copy of the variant allele. The values of \( \lambda \) used were in the set \{0.0, 0.4, 0.8, 1.2, 1.6, 2.0, 2.4\}. The trait was simulated from a mixture of normal distributions, both with constant variance 1.0.](image2)
TABLE 2. Results of tests of offspring effects of a cytochrome P-450 variant allele (CYP1A1*2A) among newborns, Montreal, Canada, May 1998–June 2000

<table>
<thead>
<tr>
<th>Trait</th>
<th>Offspring p value</th>
<th>Maternal p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)</td>
<td>0.15</td>
<td>0.54</td>
</tr>
<tr>
<td>Birth weight (z score)</td>
<td>0.63</td>
<td>0.90</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>0.28</td>
<td>0.32</td>
</tr>
</tbody>
</table>

TABLE 3. Mean values for quantitative traits by carriage of a cytochrome P-450 variant allele (CYP1A1*2A) among newborns, Montreal, Canada, May 1998–June 2000

<table>
<thead>
<tr>
<th>Trait</th>
<th>CYP1A1*2A carriage status</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)</td>
<td>Not a carrier</td>
<td>2,794</td>
</tr>
<tr>
<td></td>
<td>Carrier</td>
<td>2,920</td>
</tr>
<tr>
<td>Birth weight (z score)</td>
<td>Not a carrier</td>
<td>−0.79</td>
</tr>
<tr>
<td></td>
<td>Carrier</td>
<td>−0.68</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>Not a carrier</td>
<td>38.0</td>
</tr>
<tr>
<td></td>
<td>Carrier</td>
<td>38.4</td>
</tr>
</tbody>
</table>

these parameters produced a significant p value of 0.02. This test was based on the log-linear model with case-parent triads.

For 900 case triads and control triads, data on at least one parental genotype and the offspring genotype at the CYP1A1*2A marker were available. Within these triads, 57 percent of fathers’ genotypes were missing, while less than 1 percent of mothers’ genotypes were missing. With these families, the quantitative polytomous logistic regression model was used to verify conclusions from the described research. We first conducted simulations to estimate the type I error for a 0.05-level test based on the full model with 50 percent of the paternal genotypes missing. The estimated type I error was 0.057, which is statistically compatible with 0.05. In implementing our approach with the intraternal growth restriction data, birth weight, normalized birth weight, and gestational week (with values above 40 weeks being recoded to 40 weeks) were all considered as quantitative outcomes. The recoding of gestations lasting longer than 40 weeks was done to reflect the expectation that genetic factors related to prematurity could be quite distinct from those related to postmaturity; thus, we preferred a quantification that focused on earliness as the trait of interest. This recoding should not have affected the validity of the test. For each infant, the normalized z score was calculated by subtracting from the birth weight the mean weight for the infant’s sex and gestational length category and then dividing that difference by the corresponding category-specific standard deviation. Because cases and controls were matched on length of gestation, the birth weight z scores and gestational lengths were independent in the resulting data.

Using the framework proposed in this paper, both offspring effects and maternal effects were tested with the CYP1A1*2A variant. Both the test of offspring effects and the test of maternal effects were reduced to 1-df tests of additive effect. This was done because there was a very limited number of complete triads with the mother, father, or child having two copies of the variant (there was only one complete triad with MFC = 112 and one triad with MFC = 122). The maternal model can be reduced simply by restricting δ01 = δ12. The reduced model for additive offspring effects was described in the previous paper (4). These simplifications to additive models do not imply less validity but should be thought of as analogous to trend tests; for each test carried out, the coefficient is 0 under the corresponding null hypothesis without any added assumptions. The additive model is trivially correct under the null hypothesis, so the likelihood ratio test based on it is valid. Verifying the conclusions of the previous research, no maternal effects were found to be statistically significant. Interestingly, none of the traits were both linked and associated with the CYP1A1*2A variant. Results are shown in table 2, and arithmetic means are shown by carrier status in table 3.

DISCUSSION

When testing for maternal effects or parent-of-origin effects in quantitative trait data, few options are available. The approach suggested here extends an earlier approach for testing linkage and association between quantitative traits and diallelic markers using data from nuclear families with at least one parent and one offspring for whom the quantitative trait has been measured (4). The method can be extended to include families with additional missing data—for example, where no data on parental genotypes are available or where the offspring genotype is missing. As in the previous method, an expectation-maximization algorithm approach is used to incorporate information from incomplete triads, without assuming Hardy-Weinberg equilibrium or Mendelian transmissions. This new method is as flexible as the approach for offspring effects, in that non-normally distributed traits and admixed populations do not invalidate these tests.

Other methods in the literature require sampling siblings (7), do not allow for missing parental data (8), or are computationally intensive mixture models without available standard software (6). In addition, a method has been suggested which tests linkage and parent-of-origin effects but which requires pedigree information, or at least information on sibships (18).

While we have focused the presentation of the method on hypothesis testing, the maternal effects coefficients estimated by our approach do allow a shift interpretation when the quantitative trait is normally distributed with variance equal to 1.0. For example, the coefficient δ01 corresponds to the shift in the offspring trait distribution for a mother with one copy of the allele under study compared with mothers with no copies, for families from the 01 mating type.

When effects of the inherited genotype, maternally mediated effects, and parent-of-origin effects are all detected for a particular allele, some caution is needed in interpretation. Our three-component model implicitly assumes that these
separate genetic mechanisms act additively on the quantitative trait under study. If instead the maternal effect and the offspring-mediated effect are not additive, departures from additivity can be mistaken for parent-of-origin effects, because the maternal coefficient may depend in complex ways on the offspring genotype and the trait value. For example, consider the following possible interaction between maternal and offspring genotype. Suppose a given level of obesity in a child can be produced by the child’s inheriting a copy of the allelic variant or by the mother’s carrying a copy, which influences her own phenotype and hence the fetal development of her child. For an obese child who does not carry a copy of the variant allele, the mother will be at increased likelihood of carrying a copy herself, compared with the mother of a similarly obese child who does carry a copy. In this way, the interpretation of apparent parent-of-origin effects can become problematic.

In this paper, we have illustrated that the proposed method is valid and powerful for tests to detect maternal effects or parent-of-origin effects between a quantitative trait and a diallelic marker, with complete or incomplete triads. Readers may be interested in estimating power for scenarios other than those described here. Power can also be approximated by assuming normality of the trait, estimating the frequencies for specific strata using Hardy-Weinberg equilibrium and the assumed prevalence of the allele, and using new SAS power software available in version 9 (19).

The power of the binary logistic model may be estimated by computing the power of a two-way analysis of variance, treating the parental mating type strata as blocking factors. Because the methods are based on likelihood ratio tests, available software makes them easily programmable and the analyses quick to execute. SAS macros for carrying out such analyses are available at a National Institute of Environmental Health Sciences website (http://dir.niehs.nih.gov/dirbb/weinberg/files/qpl.htm).

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