hearing individuals with a family history of deafness. From the results of this larger study, it will be possible to see how the sample used in the article fits into a more general sample from the deaf community. Preliminary analysis of the results from the larger study shows that, although the attitudes expressed in our article are more negative than those based on the larger sample, the trends are the same. The results of this larger study are in the process of being written up for publication.

Michie and Marteau also say that we proposed that specialized counselors should be required for every disease and disability. This was not what we suggested. We advocated that language and cultural barriers could be kept to a minimum by the use of deaf genetic counselors to see deaf clients, in the same way that Asian counselors might counsel Asian clients in their own language, recognizing transcultural aspects in the genetic counseling process, rather than just the use of interpreters in this situation. We actually emphasized that it is unrealistic to suggest that only disabled people could counsel disabled clients.

A. MIDDLETON,[1,2] R. F. MUELLER,[1] AND J. HEWISON[2]
[1]*Department of Clinical Genetics, St. James's Hospital, and* [2]*School of Psychology, University of Leeds, Leeds*

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Address for correspondence and reprints: Dr. R. F. Mueller, Department of Clinical Genetics, St. James's Hospital, Beckett Street, Ashley Wing, Leeds LS9 7TF, United Kingdom. E-mail: gen6rfm@vax.bio.leeds.ac.uk

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Using Exact *P* Values to Compare the Power between the Reconstruction-Combined Transmission/ Disequilibrium Test and the Sib Transmission/ Disequilibrium Test

To the Editor:

In a recent letter in the *Journal,* Laird et al. (1998) pointed out that Spielman and Ewens's (1998) sib transmission/disequilibrium test (S-TDT) is identical to a Mantel-Haenszel test of trend. As noted by Laird et al., it is possible by this identity to use commercial software such as StatXact to calculate exact *P* values for the S-TDT. The superiority of exact *P* values over asymptotic *P* values is evident, since it is well known (e.g., see Elston 1998) that *P* values obtained on the basis of theoretical large-sample approximations can be quite unreliable if they are much smaller than .05. An example of the need of small *P* values is the association scan proposed by Risch and Merikangas (1996), which requires that *P* values $< 5 \times 10^{-8}$ be observed in order for significance to be declared.

It does not seem to be generally known that the calculation of exact *P* values for the S-TDT does not require sophisticated algorithms at all. To the contrary, it is easily incorporated into any computer program. In essence, the test statistic of the S-TDT is the total number T of alleles A (i.e., the allele of interest) in affected children in the whole sample. The null distribution of T is the convolution of all null distributions for T_i, where T_i denotes the number of alleles A in family i. The null distribution of T_i, conditional on the observed numbers n_{ai} of affected children and n_{ui} of unaffected children and on the observed marker-genotype distribution in family i, is easily calculated from a hypergeometric distribution and is concentrated on, at most, $2n_{ai} + 1$ different values. The numerical calculation of the convolution of such distributions concentrated on a small part of the natural numbers is quite feasible, at least for sample sizes typically occurring in practice (see below). The situation is very similar for the reconstruction-combined transmission/disequilibrium test (RC-TDT [Knapp 1999]), which employs reconstruction of missing parental genotypes to enhance the power of the S-TDT. This test, which does not seem to be identical to any standard statistical procedure and, therefore, requires special software for its application, also allows the calculation of exact *P* values.

I have written an SAS (SAS Institute 1990) macro that calculates exact *P* values for the S-TDT and RC-TDT, as well as *P* values based on z scores (with and without continuity correction). In order to give an impression of the time performance of this program, it was applied to allele M7 of marker D5G23 in Genetic Analysis Workshop 9 data (Hodge 1995). When all parental genotypes in these families are assumed to be unknown, 107 families remain that can be analyzed with the S-TDT and the RC-TDT. The program required less than 3 CPU-seconds for this analysis, on a low-end IBM RS6000 workstation. If each family is multiplied 10-fold (i.e., resulting in a data set of 1,070 families, which is more than the sample sizes usually occurring in practice), the SAS macro required 24 CPU-seconds.

The implementation of the RC-TDT in this macro differs, in two points, from the description given by Knapp (1999) and from the program formerly used to compare the power of the RC-TDT versus that of the

Table 1

Simulated Power of Exact S-TDT and Exact RC-TDT, for Sibships with at Least One Affected Sib (α = .001, R = 500 Replicated Samples)

	Power							
	300 Families, Each with Two Sibs		150 Families, Each with Four Sibs			100 Families, Each with Six Sibs		
				RC-TDT			RC-TDT	
Model	S-TDT	RC-TDT: Paternal Missing[a]	S-TDT	Both Missing[b]	Paternal Missing[a]	S-TDT	Both Missing[b]	Paternal Missing[a]
D1	.63	.83	.59	.64	.67	.52	.59	.61
D2	.65	.85	.86	.88	.91	.86	.90	.90
D3	.65	.92	.97	.98	.98	.98	.98	.98
A1	.64	.79	.53	.57	.60	.40	.45	.48
A2	.61	.80	.66	.72	.75	.64	.71	.73
A3	.63	.83	.80	.85	.88	.82	.85	.86
R1	.57	.60	.52	.56	.60	.40	.44	.48
R2	.61	.66	.67	.70	.71	.64	.66	.69
R3	.59	.70	.81	.82	.84	.81	.81	.81

[a] Only the paternal genotype is missing in all families.
[b] Both parental genotypes are missing in all families.

S-TDT. Both changes are related to families with marker information available for a single parent:

1. Families in which all children possess the same genotype neither allow parental-genotype reconstruction nor are suitable for S-TDT analysis. Therefore, these families were discarded from the analysis by Knapp (1999). If only a single parental marker genotype is missing and the genotype of the typed parent is *AB*, however, Curtis and Sham (1995) have shown that affected offsprings with an allele not present in the available parent (e.g., *C*) can be used for TDT analysis. The modified RC-TDT therefore includes such families. Here, the distribution of the number of alleles *A* is concentrated on the points 0 and n_{ai}, since it is required that all children in the family have the same marker genotype. (If more than one allele that is not present in the typed parent occurs in the genotype of the sibship, the missing parental genotype can be reconstructed; and, if both alleles *A* and *B* occur in the children, the family is suitable for analysis by S-TDT.)

2. Knapp (1999, p. 864) has discussed the distinction between exact reconstruction of the missing parental genotype and the condition given in his table 2, for a $BC \times AB$ mating (with the *BC* parent being typed). Inadvertently, the program used to obtain the power estimates shown in Knapp's (1999) table 5 considered a family to be reconstructable only in the case of exact reconstruction but used the null expectation and null variance as given in Knapp's table 2. Both of these values are too large for families that allow for exact reconstruction. Therefore, this bug systematically underestimates the power of the RC-TDT.

Both to compare the power of the S-TDT with the power of the RC-TDT, when rejection of the null hypothesis is based on exact *P* values for both tests, and to assess the effect of the two changes for the RC-TDT that have been described above, the same simulated samples that had been presented by Knapp (1999) were reanalyzed. When the results shown in table 1 are compared with the power estimates given in Knapp's (1999) table 5, it can be seen that *P* values based on *z* scores with continuity correction tend to be conservative. The most pronounced increase in power for families with only one missing parental genotype is observed for two sibs, in which the first of the RC-TDT changes described above could be expected to have the largest effect. (An SAS macro that calculates the S-TDT and RC-TDT test statistics and their respective exact *P* values can be obtained, by request via e-mail, from the author.)

Michael Knapp

Institute for Medical Statistics
University of Bonn
Bonn

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Address for correspondence and reprints: Dr. Michael Knapp, Institute for Medical Statistics, University of Bonn, Sigmund-Freud-Strasse 25, D-53105 Bonn, Germany. E-mail: knapp@imsdd.meb.uni-bonn.de

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