I do not think that the importance of being able to produce pedigree diagrams automatically should be minimized. Diagrams produced manually, whether using a drawing program or pen and paper, require considerable effort to produce. Inevitably, this means that when alterations need to be made one is more likely to add a few scrawled annotations than redraw them from scratch. Errors can occur in transcribing the pedigree structure or, for example, marker genotypes. The amount of information that a diagram can contain is also very limited compared to the wealth of data that may have been accumulated, and the fundamental data object consists of an individual subject rather than a pedigree. Thus, the natural way to organize data is to have a database with one record per subject, each record containing the clinical and genetic data for that subject, and enough data concerning relationships to other subjects to allow the reconstitution of the pedigree structure (for many research applications, this need consist only of pointers to the subject's parents). From such a database, one can generate both pedigree diagrams and the data files required for analyses (Cook et al. 1993), and this is not only very convenient but also guarantees that there are no inconsistencies between the diagrams and the information on which analyses are based.

In my opinion, it is highly desirable to be able to produce pedigree diagrams automatically. In light of this, I would urge that recommendations for the appearance of these diagrams take some account of what algorithms might be used generate them. The present recommendations seem to have been formulated largely with genetic counseling applications in mind, and they do not appear so appropriate for dealing with the large complex pedigrees used in linkage studies. I believe it would be premature to attempt to impose them universally.

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Reply to Marazita and Curtis

To the Editor:

We thank Dr. Marazita for her careful reading of our suggestions and appreciate her point regarding the importance of standardized nomenclature, particularly the definition of proband. Our review of the definition of proband showed a long history of imprecise definitions of the terms "proband," "index case," and "propositus/proposita." In agreement with the definition in figure 1, example *7a,* of our paper, many authors define proband as "the first family member coming to medical attention" (Bodmer and Cavalli-Sforza 1976, p. 764; Levitan 1988, p. 14; Thompson et al. 1991, pp. 58, 438; Khoury et al. 1993, p. 67; Robinson and Linden 1993, p. 573). However, not all of these authors agree that a proband must necessarily be affected with a genetic disease. If the proband is affected, these authors use "proband," "index case," and "propositus/proposita" interchangeably. Other authors define a proband as "an affected individual through whom a family is ascertained" (Morton 1959, 1982, pp. 47–48; Cavalli-Sforza and Bodmer 1971, p. 852; Kelly 1980, pp. 5–6; Thompson 1986, p. 161; Stine 1989, p. 484; Gehlehrter and Collins 1990, p. 308; Harper 1993, pp. 5, 333). These latter authors would then define an index case to be the first affected family member coming to medical attention. If the proband is unaffected, this individual would be termed the "consultand" but would not be a proband (Kelly 1980; Harper 1993).

Since there may be more than one proband per extended family (Cavalli-Sforza and Bodmer 1971; Thompson 1986; Harper 1993), we agree that "first" should not be included in the proband definition; "first" more accurately refers to an "index case." Therefore, we would like to amend our definition of "proband" in figure 1, example *7a,* to read "an affected individual coming to medical attention independent of other family members."

In reply to Dr. Curtis, we acknowledge that developing standardized ways of representing relationships on a pedigree is difficult; however, this is a challenge whether pedigrees are drawn from computer programs or by hand. Fortunately (or unfortunately, depending on your viewpoint), human relationships do not follow conventional, neat, or simple patterns. Our suggested recommendations for pedigree line definitions (fig. 3) and assisted reproductive technologies (fig. 4) may need to be modified to fit a particularly complicated family structure. For example, altering the order of birth on a pedigree should not affect interpretation if age/date of birth is included on the pedigree.

Perhaps some day all pedigrees, including clinical ped-

igrees, will be recorded directly on computer, but currently this is an impractical expense for many clinicians, and it might actually be intimidating to patients. In fact, some clinicians do not use a graphic template when constructing a pedigree in the presence of a patient for this very reason.

Several pedigree software developers were consulted during the development of the recommended standardized pedigree nomenclature. The overall response we received was that the proposed nomenclature was compatible with developing software for pedigree drawing. In light of the rapidly expanding nature of computer technology, we anticipate that the recommended symbols will become even more "computer friendly." In the meantime, it seems reasonable to begin to use the proposed pedigree nomenclature in clinical and research practice, so genetic professionals from all disciplines can "speak" the same pedigree language.

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