nature genetics

Embracing risk

In response to requests from researchers for a way to publish and credit well-executed genetic association studies regardless of the outcome, we offer an experimental solution: the journal will now consider for publication—in Analysis format—annual synopses of all adequate association studies on a particular disease or phenotype. The synopsis may be written by a consortium of the authors of unpublished but publicly deposited studies, and it is hoped that the referees of the synopses will publish their comments as a counterpoint.

Much remains to be done. First, researchers need to decide on minimally acceptable criteria for study execution and analysis. This might be done field by field, with an overall consensus to be decided by conference discussions, or a solution might evolve. For the moment, criteria can be laid out explicitly in each synopsis, explaining how the studies were chosen for inclusion. Second, authors will need to decide how to assign citable references to identify each study. If the published synopsis is to act as the primary means of assigning credit, then an accession number for each study could suffice, in the way that NCBI, GEO and ArrayExpress serve their relevant fields. One suggestion, outlined by the HuGENet group in a Commentary on p 3 of this issue, is for association studies that meet community standards to receive digital object identifiers, making them independently citable.

In addition, authors will have to decide upon a suitable database to host their studies. A number of existing databases fit the bill: HuGENet (Commentary p 3), GAD (http://geneticassociationdb.nih.gov) or the databases associated with national or regional biobanks. Ultimately, the best-funded database (or perhaps the one with the best search engine) will succeed in attracting the majority of submissions. The databases may also specialize to serve different sectors of the community (*e.g.*, PharmGKB, http://www.pharmgkb.org).

There needs to be an incentive to produce the studies to a useful standard. At the moment, only researchers interested in meta-analysis methods, which require compatible data of sufficient quality, have aimed to capture all the relevant studies. We therefore welcome suggestions, in the form of Commentaries or Correspondence, on minimum standards of statistical design and reporting, means of crediting authors of these works and incentives to make the studies publicly available. Any lasting solution must allow participation by all relevant databases and journals, and, as the HuGENet Commentary suggests, must come from the researchers themselves.

What are the benefits of this new system for the journal? As methods are developed to analyze traits influenced by multiple interacting loci (see *Nat. Genet.* **37**, 413–417; 2005), it becomes apparent that detection of association in one population and not in another (p 13 of this issue) may be expected in some situations, as in studies in which the risk conferred by a genetic variant in one population greatly exceeds that in another (p 68). Thus to concentrate only on positive results may lead us to miss an important aspect of complex diseases.

We have recently revised our criteria for genetic association studies for common and complex diseases (*Nat. Genet.* **37**, 1153; 2005) to reflect editors' and referees' increasing emphasis on accountable statistical design and transparent reporting of hypotheses, results and data processing. Nevertheless, we recognize that success in this risky field is sporadic and that not every study will fulfill all the ideal criteria. So, by providing a safety net to ensure that well-executed but negative studies and replications are not considered failures, we hope to encourage the development of community standards. These will result in positive results of biological significance as well as a genomic risk landscape within which those results can be interpreted. ■