Erratum

Human Heredity

In the article by Kotti et al., entitled 'Strategy for Detecting Susceptibility Genes with Weak or No Marginal Effect' (Hum Hered 2007;63:85–92), the Appendix was incorrect. Please find the correct Appendix below:

Appendix

A) The 2-Locus TDT for Testing Gene-Gene Interaction

We consider two biallelic markers M and N with alleles m_1 and m_2 and n_1 and n_2, respectively. There are nine possible 2-locus genotypes.

We denote:

- $\kappa_{xyzw\_x'y'z'w'}$ the number of trios in which the two parents have transmitted $m_x m_y$ and $n_z n_w$ to the affected offspring for the loci M and N, respectively and untransmitted $m_{x'} m_{y'}$ and $n_{z'} n_{w'}$ for the loci M and N, respectively.
- $\kappa_{xyzw\_.}$ the number of cases with genotypes $m_x m_y\ n_z n_w$ formed by transmitted parental gametes
- $\kappa_{.\_xyzw}$ the number of genotypes $m_x m_y\ n_z n_w$ formed by untransmitted parental gametes
- A the fact of being affected
- f_{xyzw} the penetrance of the genotype $m_x m_y\ n_z n_w$

$$f_{xyzw} = P\left(A \mid m_x m_y\ n_z n_w\right) = \frac{P\left(m_x m_y\ n_z n_w \mid A\right) P(A)}{P\left(m_x m_y\ n_z n_w\right)}$$

The likelihood of the general model is

$$L_G = \prod_{x,y,z,w} \left[P\left(m_x m_y\ n_z n_w \mid A\right)\right]^{\kappa_{xyzw\_.}}$$

$$= \prod_{x,y,z,w} \left[\frac{P\left(A \mid m_x m_y\ n_z n_w\right) P\left(m_x m_y\ n_z n_w\right)}{P(A)}\right]^{\kappa_{xyzw\_.}}$$

$P(m_x m_y\ n_z n_w)$ can be estimated in our situation by

$$\frac{\kappa_{.\_xyzw}}{K}$$

Thus,

$$L_G = \left[\frac{1}{P(A)}\right]^K \prod_{x,y,z,w} \left[f_{xyzw} \frac{\kappa_{.\_xyzw}}{K}\right]^{\kappa_{xyzw\_.}}$$

The MLE estimator of f_{xyzw} is

$$\hat{f}_{xyzw} = P(A) \frac{\kappa_{xyzw\_.}}{\kappa_{.\_xyzw}}$$

In general, the probability of being affected P(A) is not available and only the relative penetrances may be estimated.

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