

Polygenic susceptibility to breast cancer: Implications for prevention

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The knowledge of human genetic variation that will come from [studying] the human genome sequence opens up the prospect of a polygenic approach to disease prevention in which it will be possible to identify individuals as susceptible by their genotype profile and to prevent disease by targeting interventions to those at risk. However, doubts have been expressed about the magnitude of these genetic effects and, hence, the potential to apply them either to individuals or to populations. We have therefore examined the potential for prediction of risk based on common genetic variation using the results of a segregation analysis of breast and ovarian cancer occurrence in a combined dataset, including a population-based series of 1,484 breast cancer cases and 156 high-risk families from the UK (Antoniou et al., 2002). A detailed description of this segregation analysis is presented in the poster of Antoniou et al.

The polygenic model implies that genetic risk in the population has a log-normal distribution. It can also be shown that the distribution of (prior) risk in cases also comes from a log-normal distribution with the same variance as that in the population (σ^2) but with a mean that is shifted to the right by σ^2 .

Assuming all the susceptibility genes could be identified, the half of the population at highest risk would account for 88% of all cases, or the 20% of the population at lowest risk would account for just 3% of cases. In contrast, if currently identified risk factors for breast cancer were used to stratify the population, the half of the population at highest risk would account for only 62% of all cases.

These results suggest that in the future, the construction and use of genetic risk profiles may provide significant improvements in the efficacy of population-based programmes of intervention for cancers and other diseases.

References

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