

Common genetic variants, risk, and applications in cancer

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The era of genome-wide association studies has promised the discovery of many new common genetic variants that influence cancer susceptibility. The hope is that these will uncover new mechanisms in cancer development, and also allow prediction of individual risk which can be used to target screening and prevention to the individuals who can benefit most.

The common variants that have been discovered to date each confer a small increment of risk to the individual, which will in most cases not be of practical clinical value. However, a 'risk profile' constructed from a combination of risk alleles may provide a stronger discrimination, both for individual decisions about medical interventions, and for the classification of groups of individuals within the population, for example to set risk/benefit criteria for entry into national screening programmes.

Although conferring only small increases in individual risk, common variants account for a substantial fraction of cases of cancer within the population. Targetting the mechanisms by which these variants cause susceptibility is therefore in principle an approach to cancer prevention – analogous to the use of statins in cardiovascular disease. The problem is that this implies preventative treatment of a large fraction of the population for public health benefit but only small individual benefit.

I will discuss the issues around risk estimation and the application of the results, using breast cancer as an example.