Family history as a risk factor for common, complex disease - an Executive Summary

Background

Family history information is a useful tool for clinicians and medical underwriters when trying to assess an individual’s future risk of disease. Many common, complex diseases, such as cancer and stroke, are known to have strong heritable components with multicae families commonly seen. The aim of this independent, epidemiological project was to investigate the evidence on familial risks for 7 complex diseases – colorectal cancer, breast cancer, prostate cancer, lung cancer, ovarian cancer, stroke and multiple sclerosis – and to estimate absolute risks of morbidity and mortality over specific time periods.

Methodology

Systematic reviews of the medical literature were carried out to find all epidemiological studies that had attempted to estimate familial risks for each of these diseases. Relevant study details and results were extracted from each study and relative risk estimates for different categories of family history were collected. Meta-analysis was used to pool these risk estimates to produce overall risk estimates with associated confidence intervals. Subgroup analyses were implemented to explore possible causes of heterogeneity and to investigate the variation in risk with different types of affected relatives. Where available, age-stratified risk estimates were meta-analysed to produce pooled, age-specific relative risk estimates to convert into absolute risk estimates.

The age-specific relative risk estimates and UK population data on disease morbidity and mortality were input into life-tables to model their impact up to age 85. Where national incidence data were unavailable due to the lack of national registries – for stroke and multiple sclerosis – relevant data from a large, regional, prospective study were used. Absolute risk curves with confidence intervals were produced for different numbers of affected relatives and varying time periods.
Results

For colorectal cancer, breast cancer and prostate cancer more than 50 relevant studies were included in the reviews. Around 30 studies were available for lung cancer, ovarian cancer and multiple sclerosis, with over 60 on stroke. With at least one affected first-degree relative, an approximate doubling of relative risk was seen for the cancers, with a 3-4 fold increase with multiple affected relatives. The risks were marginally lower for stroke, but much higher for multiple sclerosis where a 15-fold increase was estimated with one affected relative.

Relative risks tended to be higher for younger individuals although this was not true for all diseases. As fewer studies reported age-stratified risks, there are wider confidence intervals around some of these estimates. For lung cancer and multiple sclerosis, sufficient age data were not available for pooling so overall relative risks were used in the life tables.

The absolute risk curves largely followed the population incidence curves but with higher estimates. The curves generally had narrow confidence intervals for 10- and 20-year risks which widened for lifetime risk (to age 70) curves or for age-specific curves. Where data were scarce or heterogeneous (e.g. multiple sclerosis), confidence intervals were much wider and accurate risk estimation is more difficult.

Conclusions

For common, complex diseases it is possible to accurately estimate relative and absolute familial risks. For multiple affected relatives or age-specific estimates, there is more uncertainty around the estimates due to fewer published studies. These data incorporate all the currently available evidence on familial risks for these diseases and represent best estimates of these risks.

For rarer diseases where there are fewer studies, or diseases where the background population data are not robust, it is harder to accurately estimate familial risks and to be confident in the results. More studies are needed, particularly with stratified age groups, to provide extra information. Large scale incidence data, preferably from national registries such as those used for cancers, would make absolute risk estimates more reliable and useful.