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Intergenerational transmission of cancers

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Background

About 5 to 10 percent of all cancer cases are generally attributed to heridity. One is more likely to fall victim to such a familial transmission of cancer if a parent has died of cancer, particularly if this happened at a young age. Although heredity may play a role in a relatively small number of cancer cases, the individual risk is sometimes strongly increased.

Most studies on the family history of cancers have been conducted on the basis of retrospective data, collected by means of interview. These studies are thought to suffer from a certain degree of recall or information bias. They also tend to lack statistical power due to the relatively small numbers involved, especially in the case of less common types of cancer.

Our study aims to establish any differences in the odds of young persons (<55 years) to die from cancer that might exist between the combinations of son-father, son-mother, daughter-father and daughter-mother, as observed in the total Dutch population in a 7-year period. These odds are calculated for broad age groups of parents and children, controlling for age of the child, for the following types of cancer: lung, breast, lymphatic system, large intestine, stomach, pancreas, skin, bladder, brain, oesophagus, ovary and cervix.

The calculations concern the same type of cancer in parent and child, as well as different types that are known or expected to be related, such as ovarian cancer and breast cancer. Our target population consists of all persons in the Netherlands aged 20-55 years who died of cancer in the period 1995-2001. Information on the causes of death of parents is retrieved from registers dating back to 1937.

Data and method

Two registers are linked in our study. Since 1995, Statistics Netherlands is informed on all vital events with respect to persons officially residing in the Netherlands by an automated electronic message originating from approximately 500 municipal population registers. In the event of death, the records in this first register contain demographic information on the deceased person, but do not disclose the cause(s) of death. The records furthermore contain

information on the parents if the deceased person was a native citizen (i.e., born in the Netherlands with both parents also born in the Netherlands).

Information on the cause of death is derived from the second register, containing the cause of death-declarations, which in the case of suicide are completed by a coroner. Completion of this declaration is a statutory regulation. The cause of death-declaration does not contain information to identify the deceased person. The declaration is sent to the municipal authorities in a sealed envelope, provided with a file number and forwarded to Statistics Netherlands. The cause of death is coded by Statistics Netherlands and additional demographic information is retrieved from the electronic death records which carry an identical file number. A match of the cause of death-declarations and death records shows the degree of coverage of deaths occurring to residents, whether in the Netherlands or abroad. A complete set of death records with causes of death is maintained since 1937.

In order to create a data base of children and their parents, we first selected all 75,777 native Dutch persons who died between 1 January 1995 and 31 December 2001 at ages between 20 and 55 years. Citizens of foreign origin were excluded, as information on the parents is generally not available. Of this selection, the ID-numbers, the ID-numbers of parents, the dates of birth of parents and the date of marriage of parents were retrieved from a data base on households on 1 January 1995. Persons who died after this date but who were not living in the Netherlands at the beginning of the observation period, were removed from the data set. Records of persons of foreign origin are often incomplete or unreliable with respect to information on the parents, and were therefore also excluded from the data set.
Iterative attempts were then made to link the records of parents to those of the children by means of the ID-numbers and/or dates of birth of the parents. The additional information on date of marriage was used if one of the parents could not be identified directly due to a missing key on the children's record.

Cases are children who died of (a specific type of) cancer; controls children who died of other causes. In the case of sons and fathers, we related the chance that a son who died of (a specific type of) cancer (S_c) had a father who died of (a specific type of) cancer (F_c) to the chance that a son who died of another cause (S_o) had a father who died of (a specific type of) cancer. The odds ratio for the combination son-father can be expressed as:

$$OR(c,f) = [(S_c,F_c) / (S_c,F_o)] / [(S_o,F_c) / (S_o,F_o)]$$

Odds ratios and confidence intervals were determined for each combination of parent and children and for broad age groups by binary logistic regression, using the statistical package SPSS 14.0.

First results

A detailed analysis involving all selected causes of death will be carried out in the first half of 2009. A first exploration of the data has allowed us to compare our findings to results of earlier studies. In the case of lung cancer, for example, Jonsson et al. (2004) found a 2.0 to 3.5 times increased risk of lung cancer if a parent died of lung cancer; according to Bermejo et al. (2005) the risk would be about twofold. Our data show an overall odds ratio between 1.5 and 2.0. A more detailed analysis of familial risk by age and sex (of both parent and child) indicates significant differences, pointing at a possibly more strongly increased risk for

women. This is particularly so if the mother also died at a young age (OR=4.7, 95%CI=2.1-10.5; see fig.1).

An earlier study on the familial risk of breast cancer has shown a relative risk of 2.1 (in case of a first-degree relative; Pharoah et al., 1997); the younger the affected relative, the greater the risk (Yang et al., 1998). Studies on the family history of ovarian cancer suggest an association with breast cancer risk, but the evidence is inconclusive. A first-degree relative with ovarian cancer confers a modestly increased risk of breast cancer (OR=1.3; Kerber and Slattery, 1995), but other studies have found no evidence of increased risk (Negri et al., 1997). Our data show a similarly increased risk of breast cancer in case of a mother who also died of breast cancer (OR=2.2, 95%CI=1.8-2.6); the risk is furthermore higher if the mother died before the age of 55 years (OR=3.3, 95%CI=2.3-4.8; see fig.2). Our data confirm the relationship between ovarian cancer of the mother and breast cancer of the daughter, demonstrated by Kerber and Slattery. This risk is less strongly increased (OR=1.7, 95%CI=1.3-2.2) than that of breast cancer of the mother, but higher than shown by Kerber and Slattery. As in the case where the mother died of breast cancer, the risk of breast cancer of the daughter appears to be higher if the mother died of ovarian cancer before age 55 (OR=2.7, 95%CI=1.4-5.0).

Literature

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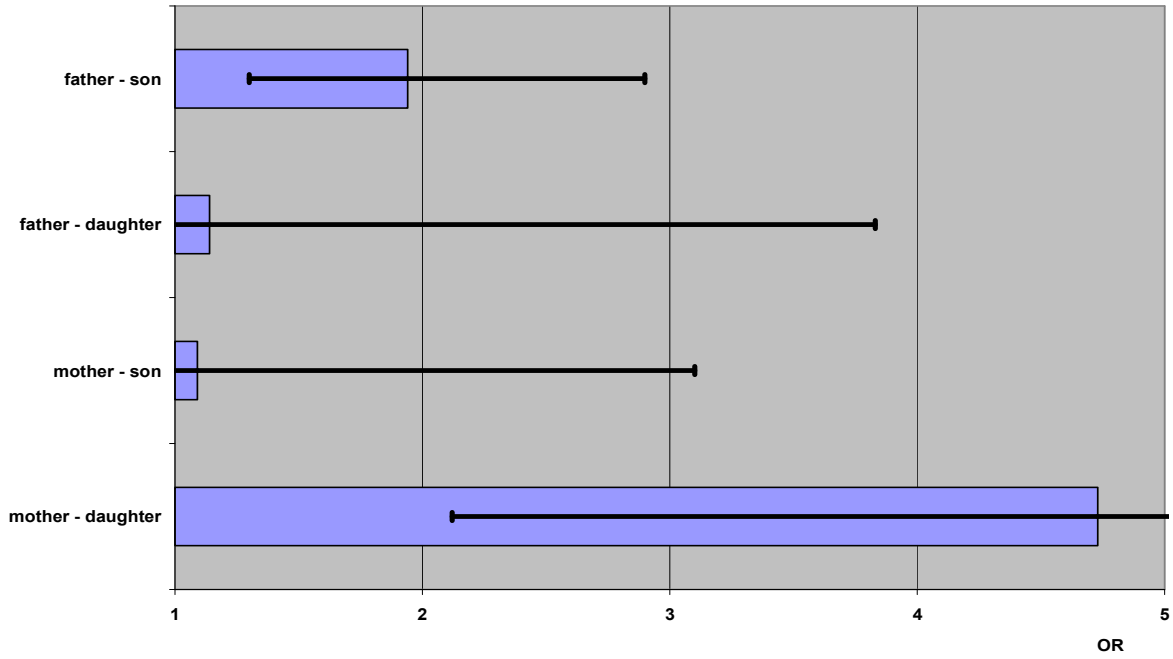
1. Familial risk, the Netherlands (OR; 95%CI)
Lung cancer, parents <55 years



2. Familial risk, the Netherlands (OR; 95%CI)
Breast cancer