Familial association of pancreatic cancer with other malignancies in Swedish families

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BACKGROUND: The aim of this study was to characterise the familial association of pancreatic cancer with other malignancies.

METHODS: Relative risks (RRs) of pancreatic cancer according to family history of cancer were calculated using the updated Swedish Family-Cancer Database, which includes over 11.5 million individuals. Estimates were based on Poisson regression. RRs of tumours for individuals with a parental history of pancreatic cancer were also estimated.

RESULTS: The risk of pancreatic cancer was elevated in individuals with a parental history of cancers of the liver (RR 1.41; 95% CI 1.10–1.81), kidney (RR 1.37; 95% CI 1.06–1.76), lung (RR 1.50; 95% CI 1.27–1.79) and larynx (RR 1.98; 95% CI 1.19–3.28). Associations were also found between parental history of pancreatic cancer and cancers of the small intestine, colon, breast, lung, testis and cervix in offspring. There was an increased risk of pancreatic cancer associated with early-onset breast cancer in siblings.

CONCLUSION: Pancreatic cancer aggregates in families with several types of cancer. Smoking may contribute to the familial aggregation of pancreatic and lung tumours, and the familial clustering of pancreatic and breast cancer could be partially explained by inherited mutations in the BRCA2 gene.

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Pancreatic cancer is the fourth most common cause of death from cancer in Sweden (Hemminki and Li, 2003a; Linder et al., 2007). Prognosis for patients with this disease is very poor: the median survival time is 6 months and the 5-year survival rate is below 10% (Rulyak and Brentnall, 2004; Ghaneh et al., 2007; Linder et al., 2007). Early treatment of pancreatic cancer increases the likelihood of survival (Greenhalf and Neoptolemos, 2006). However, most patients are diagnosed at an advanced stage (Klein et al., 2002; Greer et al., 2007). Studying the familial clustering of pancreatic cancer with non-pancreatic malignancies meets two objectives: it provides information for cancer risk assessment in genetic counselling and provides clues with regard to the aetiology of the disease.

Around 4% of patients diagnosed with pancreatic cancer have parents or siblings who are also affected by pancreatic cancer (Hemminki et al., 2008). It has been estimated that up to 20% of the familial clustering of pancreatic cancer can be attributed to syndromes such as hereditary non-polyposis colon cancer (HNPCC), familial adenomatous polyposis and familial atypical multiple mole melanoma syndrome (Klein et al., 2001; Jaffe et al., 2002). The corresponding genes associated with these disorders are mismatch repair genes, APC and CDKN2A (Klein et al., 2001; Lynch and de la Chapelle, 2003). Other reported risk factors for the disease are tobacco smoking, obesity and diet rich in calories and meat (Coughlin et al., 2000; Chiu et al., 2001; Michaud et al., 2001; MacLeod and Chowdhury, 2006; Ghaneh et al., 2007).

The present population-based study used the Swedish Family-Cancer Database. An important advantage of the database is that information on familial relationships and cancers comes from registered sources of practically complete coverage, thus offering unique possibilities for precise and unbiased assessment. The risks of pancreatic cancer were estimated according to family history of the most prevalent types of cancer. Risks of non-pancreatic malignancies for individuals with a family history of pancreatic cancer were also calculated. The database has been used previously to assess the association of pancreatic cancer with parental history of cancers from 1961 to 1998 (Hemminki and Li, 2003a). The database was updated in 2006 and now includes over 1.2 million tumours diagnosed between 1958 and 2004. Compared with the previous version, the number of pancreatic cancer patients with a parental history of the disease increased from 34 to 84 patients. Using the updated database, we explored the risk of pancreatic cancer according to sibling history of cancer as well. As early age of onset has been a reported characteristic of hereditary cancer, we additionally calculated the relative risks of pancreatic cancer according to the parental/sibling age of diagnosis of cancer (Krainer et al., 1997; Raimondi et al., 2007).

PATIENTS AND METHODS

Data on the incidence of pancreatic cancer between 1961 and 2004 in Sweden were derived from the Nordcan Database (Engholm
et al, 2008). Relative risks of pancreatic and other cancers were calculated using the updated Swedish Family-Cancer Database. The population-based Swedish Family-Cancer Database was created by linking the Multigeneration Register at Statistics Sweden to the Swedish Cancer Registry (Hemminki et al, 2001). The Multigeneration Register includes individuals born in Sweden after 1931 and their biological parents. The Swedish Cancer Registry is based on compulsory reports about patients provided by pathologists and cytologists, who report every cancer diagnosis on surgically removed tissues, biopsies, cytological specimens, bone marrow aspirates and autopsies (Center for Epidemiology, 2004). The latest update of the database comprises more than 11.5 million individuals. Data on patients with cancer were retrieved from the Swedish Cancer Registry from 1961 to 2004. The coverage of the database is practically complete; however, some familial links are missing from offspring who were born before 1941 and who died between 1960 and 1997. The effect of the missing data is a reduced number of mortal cancers among offspring. This is unlikely to cause bias to familial studies because familial and sporadic cases would be reduced proportionately (Hemminki et al, 1998; Hemminki and Vaittinen, 1999). This study relies on individuals who had information available about both parents. Family history was restricted to first-degree relatives, that is, to parents and siblings.

Follow-up started from the date of birth, immigration or from 1 January 1961, whichever occurred last. Follow-up ended on the date of diagnosis of first cancer, on death, emigration or on the closing date of the study (31 December 2004), whichever came first. Cases of cancer and person-years were classified according to gender, family history of cancer, calendar year, age, socioeconomic status and geographical region. The distribution of the number of cases in each group was modelled by Poisson regression. We controlled for family history of cancer, gender, calendar year, age, socioeconomic status and geographical region in all models. In addition, dichotomous variables were created according to parental/sibling age of diagnosis with cancer (0–55; 56–71; 72 or older).

The Genmod procedure of SAS software was used for the analysis (SAS Version 9.1; SAS Institute, Cary, NC, USA). Standard Poisson regression assumes independent observations. To account for the possible overdispersion because of a clustered family structure, s.e. can be adjusted using Pearson’s $\chi^2$-test, divided by degrees of freedom. The adjustment results in slightly wider confidence intervals. For example, the relative risk (RR) of pancreatic cancer for individuals with a family history of pancreatic cancer was 2.11 (95% CI = 1.67–2.66) after adjustment and 2.11 (95% CI = 1.73–2.57) without adjustment. However, this procedure may be particularly sensitive to outlying observations that are expected in our large data set. Therefore, we show in this article unadjusted CIs and point to the possibility of conservative limits due to familial dependence. The tables in this study show only cancer sites with significant results or with at least 30 affected parent–offspring pairs.

Risk of pancreatic cancer in hereditary pancreatitis was analysed by identifying hospitalised cases of chronic pancreatitis through the Swedish Hospital Discharge Register, containing all hospitalisations in Sweden between 1961 and 2007, but with a nationwide coverage only since 1987 (for description, see (Hemminki et al, 2009)). Familial pancreatitis was defined when at least two family members were hospitalised with this disease. Pancreatic cancers in any family members were scored through the Cancer Registry. Similarly, patients hospitalised for cystic fibrosis were identified and their subsequent pancreatic cancers were retrieved from the Cancer Registry.

RESULTS

Age-standardised incidence of pancreatic cancer in Sweden in the period 1961–2004 is shown in Figure 1. The incidence of pancreatic cancer in this period is stable, except from a spike in the early 1970s among men. The proportion of pancreatic cancer patients with a parent or sibling affected by the disease was 3.66% (N = 103).

Table 1 provides the results of a multivariate Poisson regression that included a dichotomous variable for family history of pancreatic cancer diagnosed at any age, in addition to gender, calendar year, age, socioeconomic status and geographical region: women were at a slightly lower risk of pancreatic cancer compared with men (RR 0.86; 95% CI 0.75–0.97). As expected, age was found to be associated with the risk of developing pancreatic cancer. The risk of pancreatic cancer was increased among individuals with a family history of the malignancy (RR 2.11; 95% CI 1.73–2.57). Individuals with a parent diagnosed with pancreatic cancer are at an increased risk of developing pancreatic cancer (RR 1.93; 95% CI 1.55–2.40) (Table 2). There was an increased risk of pancreatic cancer among the offspring of patients with cancers of the liver (RR 1.41; 95% CI 1.10–1.81), larynx (RR 1.98; 95% CI 1.19–3.28), lungs (RR 1.50; 95% CI 1.27–1.79) and kidneys (RR 1.37; 95% CI 1.06–1.76).

In contrast, we also examined the risk of tumours in the offspring of pancreatic cancer patients (Table 3). There was an increased risk of cancer of the small intestine (RR 1.62; 95% CI 1.02–2.55) and colon (RR 1.28; 95% CI 1.10–1.48) among those with a parental history of pancreatic cancer. Parental pancreatic cancer was associated with an increased risk of melanoma in the offspring (RR 1.25; 95% CI 1.10–1.42). The offspring of patients with pancreatic cancer were at a higher risk of cancers of the liver (RR 1.52; 95% CI 1.17–1.98), lung (RR 1.18; 95% CI 1.02–1.36) and the breast (RR 1.21; 95% CI 1.13–1.31). Women with a parental history of pancreatic cancer had an increased risk of developing cervical cancer (RR 1.44; 95% CI 1.18–1.76). Sons of
patients with pancreatic cancer had an elevated risk of cancers of the testis (RR 1.35; 95% CI 1.06–1.73) and other male genital organs (RR 1.88; 95% CI 1.06–3.34). The risk of Hodgkin’s disease was elevated among those individuals whose parent was diagnosed with pancreatic cancer after the age of 71 years (RR 1.67; 95% CI 1.04–2.69). Parental history of pancreatic cancer after the age of 71 years (RR 1.67; 95% CI 1.04–2.69) (Table 4). The risk of familial aggregation of pancreatic cancer offers a unique opportunity to advance our understanding of pancreatic cancer development. An advantage of this study was that data on familial relationships were obtained from registered sources and tumour diagnoses were histologically confirmed, excluding any type of recall bias. The updated Swedish Family-Cancer Database permitted us to study pancreatic cancer risk not only according to parental but also according to sibling history of cancer.

The small estimated proportion of familial cases of pancreatic cancer in our dataset (3.66%) was in accordance with earlier calculations (Hemminki et al., 2008).

**DISCUSSION**

Studying the familial aggregation of pancreatic cancer offers a unique opportunity to advance our understanding of pancreatic cancer development. An advantage of this study was that data on familial relationships were obtained from registered sources and tumour diagnoses were histologically confirmed, excluding any type of recall bias. The updated Swedish Family-Cancer Database permitted us to study pancreatic cancer risk not only according to parental but also according to sibling history of cancer.

The small estimated proportion of familial cases of pancreatic cancer in our dataset (3.66%) was in accordance with earlier calculations (Hemminki et al., 2008).
Table 3 Relative risk of tumours (RR) for the offspring of individuals affected by pancreatic cancer

| Offspring cancer site | N   | RR (95% CI) | N   | RR (95% CI) | N   | RR (95% CI) | N   | RR (95% CI) |
|-----------------------|-----|-------------|-----|-------------|-----|-------------|-----|-------------|
| Upper aerodigestive tract | 60 | 1.25 (0.97–1.61) | 6 | 1.41 (0.63–2.15) | 35 | 1.63 (1.16–2.27) | 19 | 0.87 (0.55–1.36) |
| Salivary glands | 18 | 2.06 (1.29–3.29) | 2 | 1.63 (0.41–6.52) | 15 | 1.90 (1.14–3.16) | 4 | 0.45 (0.17–1.19) |
| Oesophagus | 21 | 1.16 (0.75–1.79) | 2 | 1.37 (0.93–2.03) | 5 | 0.95 (0.39–2.28) | 13 | 2.38 (1.38–4.13) |
| Stomach | 47 | 1.13 (0.85–1.51) | 5 | 0.79 (0.33–1.89) | 51 | 1.33 (1.01–1.75) | 42 | 0.98 (0.72–1.32) |
| Small intestine | 19 | 1.62 (1.02–2.55) | 5 | 1.80 (0.75–4.33) | 28 | 1.69 (1.16–2.46) | 25 | 1.34 (0.90–1.99) |
| Colon | 182 | 1.10 (1.10–1.48) | 15 | 1.34 (0.81–2.23) | 79 | 1.27 (1.01–1.58) | 88 | 1.29 (1.04–1.60) |
| Rectum | 98 | 1.11 (0.91–1.36) | 5 | 0.79 (0.33–1.89) | 51 | 1.33 (1.01–1.75) | 42 | 0.98 (0.72–1.32) |
| Liver | 58 | 1.52 (1.17–1.98) | 5 | 1.80 (0.75–4.33) | 28 | 1.69 (1.16–2.46) | 25 | 1.34 (0.90–1.99) |
| Pancreas | 84 | 1.93 (1.55–2.40) | 10 | 3.32 (1.78–6.18) | 41 | 2.19 (1.61–2.98) | 33 | 1.54 (1.09–2.17) |
| Larynx | 15 | 1.26 (0.75–2.10) | 76 | 1.21 (1.13–1.31) | 75 | 1.32 (1.05–1.66) | 361 | 1.33 (1.20–1.48) |
| Lung | 191 | 1.18 (1.02–1.36) | 19 | 1.66 (1.06–2.61) | 82 | 1.17 (0.94–1.45) | 90 | 1.13 (0.92–1.39) |
| Breast | 726 | 1.31 (1.13–1.51) | 7 | 1.35 (0.78–2.33) | 55 | 1.61 (1.24–2.10) | 33 | 1.28 (0.91–1.81) |
| Cervix uteri | 101 | 1.44 (1.18–1.76) | 13 | 1.35 (0.78–2.33) | 41 | 1.05 (0.77–1.43) | 61 | 1.33 (1.04–1.72) |
| Endometrium | 107 | 1.18 (0.97–1.42) | 5 | 0.80 (0.33–1.91) | 51 | 1.30 (0.99–1.71) | 42 | 1.09 (0.80–1.48) |
| Ovary | 104 | 1.20 (0.99–1.45) | 11 | 1.30 (0.72–2.35) | 51 | 1.12 (0.96–1.32) | 154 | 0.94 (0.80–1.10) |
| Prostate | 316 | 1.01 (0.90–1.12) | 11 | 1.07 (0.73–1.57) | 38 | 1.57 (1.14–2.16) | 19 | 1.22 (0.78–1.92) |
| Testis | 65 | 1.35 (1.06–1.73) | 8 | 1.04 (0.52–2.07) | 5 | 1.70 (0.71–4.12) | 7 | 2.43 (1.15–5.13) |
| Other male genital organs | 12 | 1.88 (1.06–3.34) | 59 | 0.98 (0.77–1.25) | 31 | 1.02 (0.72–1.45) | 35 | 1.09 (0.78–1.51) |
| Kidney | 67 | 0.98 (0.77–1.25) | 8 | 1.09 (0.55–2.19) | 47 | 1.08 (0.81–1.44) | 55 | 1.15 (0.89–1.51) |
| Urinary organs | 110 | 1.11 (0.92–1.34) | 8 | 1.09 (0.55–2.19) | 47 | 1.08 (0.81–1.44) | 55 | 1.15 (0.89–1.51) |
| Melanoma | 241 | 1.25 (1.10–1.42) | 32 | 1.47 (1.04–2.08) | 133 | 1.47 (1.24–1.74) | 76 | 0.96 (0.77–1.21) |
| Squamous cell skin | 65 | 1.06 (0.83–1.35) | 5 | 1.02 (0.43–2.46) | 27 | 0.99 (0.68–1.45) | 33 | 1.13 (0.81–1.60) |
| Eye | 5 | 0.78 (0.32–1.88) | 2 | 0.68 (0.17–2.71) | 3 | 1.06 (0.34–3.29) |
| Nervous System | 151 | 0.98 (0.84–1.15) | 21 | 1.13 (0.74–1.74) | 61 | 0.84 (0.66–1.09) | 69 | 1.10 (0.81–1.40) |
| Thyroid gland | 35 | 0.83 (0.59–1.16) | 8 | 1.49 (0.74–2.97) | 14 | 0.69 (0.41–1.17) | 13 | 0.80 (0.46–1.38) |
| Endocrine glands | 93 | 1.28 (1.04–1.57) | 15 | 1.96 (1.18–3.26) | 40 | 1.19 (0.87–1.62) | 38 | 1.22 (0.89–1.68) |
| Connective tissue | 25 | 0.99 (0.67–1.48) | 3 | 0.99 (0.32–3.06) | 9 | 0.76 (0.39–1.46) | 13 | 1.28 (0.74–2.21) |
| Non-Hodgkin’s lymphoma | 115 | 1.14 (0.94–1.37) | 14 | 1.46 (0.87–2.47) | 51 | 1.11 (0.84–1.46) | 50 | 1.10 (0.83–1.45) |
| Hodgkin’s disease | 34 | 1.16 (0.82–1.62) | 6 | 1.35 (0.61–3.02) | 11 | 0.77 (0.43–1.39) | 17 | 1.67 (1.04–2.69) |
| Leukaemia | 88 | 1.03 (0.84–1.27) | 10 | 1.03 (0.56–1.92) | 45 | 1.13 (0.85–1.52) | 33 | 0.90 (0.64–1.27) |

Bold signifies \( P < 0.05 \).
cases were diagnosed 50 or more years after the diagnosis of pancreatitis (Howes et al., 2004). However, our maximal follow-up time was 43 years, of which only 21 years were with a full national coverage, decreasing the chances of finding a relationship between the two diseases. Pancreatic cancer is a rare complication after cystic fibrosis and the risk of estimation has been based on international case collections (Maisonpierre et al., 2007).

A potential limitation of our study was the unavailability of information on other potential risk factors of pancreatic cancer such as tobacco smoking, alcohol consumption and diet. It is important to note that some of the significant associations could be attributed to chance as well. Our investigation was also limited by the small number of tumours at some locations. The problem could be alleviated when future updates of the Swedish Family-Cancer Database are available.

The present results on the aggregation of pancreatic cancer with other cancers in Swedish families suggest that pancreatic cancer shares a genetic and/or environmental aetiology with cancer at several sites. The results of this study demonstrated a familial association of pancreatic tumours with cancers of the lung, liver and kidney. An association was also found between pancreatic cancer in parents and melanoma in offspring. Individuals with a parental history of pancreatic cancer showed an increased risk of small intestine, colon, lung, breast, testicular and cervical cancers. There was an elevated risk of pancreatic cancer among those whose sibling had lung cancer before the age of 56 years. Some of the observed associations might be related to smoking and mutations in genes such as BRCA2.

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Conflict of interest

The authors declare no conflict of interest.

REFERENCES

Agalliu I, Karlins E, Kwon EM, Iwasaki LM, Diamond A, Ozrander EA, Stanford JL (2007) Rare germline mutations in the BRCA2 gene are associated with early-onset prostate cancer. Br J Cancer 97: 826–831.

Center for Epidemiology (2004) Cancer Incidence in Sweden 2002. The National Board of Health and Welfare: Stockholm.

Chiu BC, Lynch CF, Cerhan JR, Cantor KP (2001) Cigarette smoking and risk of bladder, pancreas, kidney, and colorectal cancers in Iowa. Ann Epidemiol 11: 28–37.

Familial aggregation of pancreatic tumours

E Hiripi et al

Table 4  Relative risk of pancreatic cancer (RR) diagnosed in siblings of individuals affected by cancer

| Sibling cancer site | Any age | N | RR (95% CI) | 0–55 | N | RR (95% CI) | 56–71 | N | RR (95% CI) |
|---------------------|---------|---|-------------|------|---|-------------|------|---|-------------|
| Upper aerodigestive tract | 8 | 1.28 (0.64 – 2.57) | 6 | 2.03 (0.91 – 4.53) | 2 | 0.61 (0.15 – 2.45) |
| Oesophagus | 8 | 3.39 (1.69 – 6.79) | 2 | 3.16 (0.79 – 12.6) | 6 | 3.49 (1.57 – 7.77) |
| Stomach | 9 | 1.35 (0.70 – 2.59) | 3 | 1.13 (0.36 – 3.50) | 6 | 1.51 (0.68 – 3.37) |
| Colon | 18 | 0.96 (0.60 – 1.53) | 7 | 0.96 (0.46 – 2.01) | 11 | 0.96 (0.53 – 1.74) |
| Rectum | 13 | 1.09 (0.63 – 1.89) | 3 | 0.69 (0.22 – 2.15) | 10 | 1.32 (0.71 – 2.46) |
| Liver | 11 | 2.07 (1.15 – 3.75) | 9 | 5.06 (2.63 – 9.74) | 10 | 2.47 (1.33 – 4.59) |
| Pancreas | 19 | 3.26 (2.07 – 5.12) | 9 | 5.06 (2.63 – 9.74) | 10 | 2.47 (1.33 – 4.59) |
| Larynx | 2 | 1.11 (0.28 – 4.46) | 13 | 1.74 (1.01 – 3.00) | 12 | 0.77 (0.44 – 1.37) |
| Lung | 25 | 1.09 (0.73 – 1.61) | 3 | 0.88 (0.28 – 2.72) | 8 | 1.09 (0.41 – 2.90) |
| Breast | 88 | 1.19 (0.96 – 1.48) | 59 | 1.37 (1.06 – 1.77) | 29 | 0.95 (0.66 – 1.38) |
| Cervix uteri | 7 | 0.79 (0.38 – 1.65) | 6 | 0.79 (0.35 – 1.75) | 3 | 0.59 (0.19 – 1.84) |
| Endometrium | 18 | 1.50 (0.95 – 2.39) | 8 | 1.68 (0.84 – 3.36) | 10 | 1.39 (0.75 – 2.59) |
| Ovary | 11 | 0.95 (0.52 – 1.71) | 9 | 1.26 (0.66 – 2.43) | 2 | 0.45 (0.11 – 1.82) |
| Prostate | 47 | 1.19 (0.89 – 1.59) | 9 | 2.36 (1.23 – 4.54) | 38 | 1.07 (0.77 – 1.47) |
| Testis | 4 | 1.09 (0.41 – 2.90) | 3 | 0.88 (0.28 – 2.72) | 8 | 1.09 (0.41 – 2.90) |
| Other male genital organs | 3 | 3.57 (1.15 – 11.1) | 3 | 6.48 (2.09 – 20.1) | 3 | 6.48 (2.09 – 20.1) |
| Kidney | 11 | 1.17 (0.65 – 2.11) | 8 | 1.86 (0.93 – 3.73) | 3 | 0.59 (0.19 – 1.84) |
| Urinary organs | 17 | 1.24 (0.77 – 2.00) | 9 | 1.64 (0.85 – 3.16) | 8 | 0.98 (0.49 – 1.96) |
| Melanoma | 19 | 0.94 (0.60 – 1.48) | 13 | 0.98 (0.57 – 1.69) | 6 | 0.88 (0.39 – 1.95) |
| Squamous cell skin | 10 | 1.31 (0.70 – 2.44) | 4 | 1.31 (0.49 – 3.49) | 6 | 1.31 (0.59 – 2.93) |
| Eye | 3 | 3.26 (1.05 – 10.1) | 3 | 4.70 (1.52 – 14.6) | 5 | 0.80 (0.33 – 1.93) |
| Nervous system | 15 | 0.88 (0.53 – 1.45) | 10 | 0.92 (0.49 – 1.71) | 5 | 0.80 (0.33 – 1.93) |
| Endocrine glands | 13 | 1.38 (0.80 – 2.39) | 5 | 0.81 (0.34 – 1.95) | 8 | 2.51 (1.25 – 5.02) |
| Connective tissue | 9 | 3.12 (1.62 – 6.00) | 5 | 2.70 (1.12 – 6.50) | 4 | 3.87 (1.45 – 10.3) |
| Hodgkin’s disease | 3 | 1.08 (0.35 – 3.36) | 3 | 1.25 (0.40 – 3.89) | 4 | 0.63 (0.24 – 1.69) |
| Non-Hodgkin’s lymphoma | 10 | 0.76 (0.41 – 1.41) | 6 | 0.87 (0.39 – 1.95) | 4 | 0.63 (0.24 – 1.69) |
| Leukaemia | 8 | 0.88 (0.44 – 1.75) | 7 | 1.54 (0.73 – 3.24) | 7 | 1.54 (0.73 – 3.24) |

Bold signifies P < 0.05.
Familial aggregation of pancreatic tumours

E Hirpi et al.

Klein AP, Beaty TH, Bailey-Wilson JE, Brune KA, Hruban RH, Petersen GM (2002) Evidence for a major gene influencing risk of pancreatic cancer. *Genet Epidemiol* 23: 133–149

Klein AP, Hruban RH, Brune KA, Petersen GM, Goggins M (2001) Familial pancreatic cancer. *Cancer* 7: 266–273

Krainer M, Silva-Arrieta S, Fitzgerald MG, Shimada A, Ishioka C, Kanamaru R, MacDonald DJ, Unsal H, Finkelstein DM, Bowcock A, Isselbacher KJ, Haber DA (1997) Differential contributions of BRCA1 and BRCA2 to early-onset breast cancer. *New Engl J Med* 336: 1416–1421

Lerch MM (2006) Anticipating disaster: the genetics of familial pancreatic cancer. *Gut* 55: 150–151

Linder S, Bostrom L, Nilsson B (2007) Pancreatic carcinoma incidence and survival in Sweden in 1980–2000: a population-based study of 16,758 hospitalized patients with special reference to different therapies. *Eur J Surg Oncol* 33: 616–622

Lorenzo Bermejo J, Hemminki K (2004) Familial association of histology specific breast cancers with cancers at other sites. *Int J Cancer* 109: 430–435

Lynch HT, de la Chapelle A (2003) Hereditary colorectal cancer. *New Engl J Med* 348: 919–932

MacLeod SL, Chowdhury P (2006) The genetics of nicotine dependence: relationship to pancreatic cancer. *World J Gastroenterol* 12: 7433–7439

Maisonneuve P, Marshall BC, Lowenfels AB (2007) Risk of pancreatic cancer in patients with cystic fibrosis. *Gut* 56: 1327–1328

McFaul CD, Greenhalf W, Earl J, Howes N, Neoptolemos JP, Kress R, Sina-Frey M, Rieder H, Hahn S, Bartisch DK (2006) Anticipation in familial pancreatic cancer. *Gut* 55: 252–258

McWilliams RR, Rabe KG, Olswold C, De Andrade M, Petersen GM (2005) Risk of malignancy in first-degree relatives of patients with pancreatic carcinoma. *Cancer* 104: 388–394

Michaud DS, Giovannucci E, Willett WC, Colditz GA, Stampfer MJ, Giovannucci EL, Hunter DJ, Rimm EB, Willett WC, Speizer FE (1996) A prospective study of cigarette smoking and the risk of pancreatic cancer. *Arch Int Med* 156: 2235–2260

Gayther SA, Ponder BA (1997) Mutations of the BRCA1 and BRCA2 genes and the possibilities for predictive testing. *Mal Med Today* 3: 168–174