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Familial transmission of prostate, breast and colorectal cancer in adoptees is related to cancer in biological but not in adoptive parents: A nationwide family study

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Abstract ***Aim:*** Familial clustering of prostate, breast and colorectal cancer is well established, but the familial risk of these cancers has not been determined among adoptees. The aim was to disentangle the contributions of genetic and environmental factors to the familial transmission of prostate, breast and colorectal cancer.
Methods: The Swedish Multi-Generation Register was used to follow all adoptees born between 1932 and 1969 ($n = 70{,}965$) for prostate, breast and colorectal cancer from January 1958 up to December 2010. The risk of prostate, breast and colorectal cancer was estimated in adoptees with at least one biological parent with the same cancer type compared with adoptees without a biological parent with the same cancer type. The risk of cancer was also determined in adoptees with at least one adoptive parent with cancer compared with adoptees with an adoptive parent without cancer.
Results: Adoptees with at least one biological parent with prostate, breast or colorectal cancer were more likely to have cancer of the same type than adoptees with biological parents not affected by these respective cancer types (standardised incidence ratio = SIR: 1.8 [95% confidence interval 1.2–2.7], 2.0 [1.6–2.5] and 1.9 [1.2–2.9], respectively). In contrast, adoptees with at least one adoptive parent with prostate, breast or colorectal cancer were not at an increased risk of these respective cancer types (SIR = 1.2 [0.94–1.6], 0.97 [0.71–1.3], and 1.1 [0.71–1.5], respectively).
Conclusions: The findings of the study support the importance of genetic/biological factors in the familial transmission of prostate, breast and colorectal cancer.
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1. Introduction

Family history of prostate, breast and colorectal cancers is a well-established risk factor for these cancers [1]. In Sweden prostate cancer shows the highest familial proportion of 20%, followed by breast (14%) and colorectal (13%) cancers [2]. Although an increasing number of cancer susceptibility genes have been identified for prostate, breast and colorectal cancer [3–8], it is not determined whether the increased familial risks reported for breast, prostate or colorectal cancer are related to genetic (biological) or environmental factors. It is increasingly appreciated that lifestyle factors may contribute to an increased cancer risk [9,10], but to what extent they contribute to the increased familial risks reported for prostate, breast or colorectal cancer is not known. Segregation analyses in families have indicated that genetic factors are important contributors to the familial risk [11–16]. Twin studies have also shown a significant heritability for prostate, breast and colorectal cancer [17–20]. However, it is difficult to disentangle the contributions of genetic and family environmental factors in family studies of cancer because most children, including dizygotic (DZ) and monozygotic twins (MZ), grow up in their biological families [21–23]. The most critical assumption in twin studies is that MZ and DZ twins show similarities because of the sharing of environmental factors, so that the difference in concordance rates between MZ and DZ twins is only a reflection of genetic factors [23]. Another possible avenue for studying whether genetic and family environmental factors have differential influences on the transmission of cancer is a follow-up study of a large sample of adoptees [12]. Studies of adoptees offer a unique opportunity to study the genetic transmission of cancer because adoptees do not grow up in their biological families [23]. Transmission of cancer from biological parents to offspring would therefore be explained by genetic factors rather than family environment. In addition, transmission of cancer from adoptive parents to their non-biological offspring would be explained by family environment rather than genetic factors.

The Swedish Multi-Generation Register consists of data on more than nine million individuals born from 1932 onwards [24–26]. Information is available on mothers in 97% and on fathers in 95% of index persons [24–26]. In a previous study of coronary heart disease (CHD) among adoptees it was possible to identify 80,214 Swedish-born adoptees who were linked to their biological parents as well as to their adoptive parents [27].

1.1. Aims

To the best of our knowledge, no previous study of familial transmission of prostate, breast and colorectal cancer has focused on adoptees. This study uses a subset of the Swedish Cancer Register [28–30] and the Swedish Multi-Generation Register [24–26], which links all adoptees born in Sweden between 1932 and 1969 to their biological and adoptive parents. Cancer diagnoses for prostate, breast and colorectal cancer for parents and adoptees were identified from January 1958 up to December 2010. The study had two aims: (1) to examine the risk of prostate, breast and colorectal cancer in adoptees with at least one biological parent affected by the same type of cancer, and (2) to examine the risk of prostate, breast and colorectal cancer in adoptees with at least one adoptive parent affected by the same cancer type. The control groups consisted of adoptees without a biological parent affected by the same cancer type (first aim), and adoptees without an adoptive parent affected by the same cancer type (second aim).

2. Material and methods

2.1. Data sources

The dataset used in this study was constructed by linking the total population register, the Multi-Generation Register, the Swedish Cancer Register and the Swedish Cause of Death Register provided by Statistics Sweden and the National Board of Health and Welfare [24–26,28–30]. Information from various registers in the database is linked at the individual level via the national 10-digit civic registration number assigned to each resident in Sweden for his or her lifetime. Prior to inclusion in the dataset, civic registration numbers were replaced by serial numbers to preserve the anonymity of all individuals. Using these linked data, we were able to identify our study population—70,965 Swedish-born adoptees born between 1932 and 1969—and to link them to their biological and adoptive parents [26]. It was possible to link 87% of the total population of adoptees to their biological as well as their adoptive parents. Adoptees were excluded if we could not link them to any of their biological parents or any of their adoptive parents. Adoptees were also excluded if data on birth year were missing, if adoptees emigrated before start of follow-up, or if the adoptive parents and the biological parent had the same identification number.

The analyses were limited to Swedish-born individuals because first-generation immigrants cannot be linked to their biological parents if the latter are not registered in Sweden. Data were not available about age at adoption. However, from other sources we know that most adoptions were previously made from unwanted pregnancies in young unmarried women [31–33]. The children were taken into institutional care by the municipalities shortly after birth to be adopted at a median age of 6 months, and few children were adopted at a later age than 12 months [31–33]. Boys tended to be adopted

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