

Short Report

Reduced incidence of cervical cancer in mothers of sons with allergic rhinoconjunctivitis, asthma or eczema

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Abstract

Because infection with human papillomavirus is a necessary cause of cervical cancer, it is likely that host immunological factors involved in defense against such infections are important for susceptibility to this cancer. By examining associations between allergy in sons and cervical cancer in their mothers, we aimed to test for genetic components involved in both allergy and cervical cancer development. Women born in Sweden between 1932 and 1960 with at least 1 son with medical records from military conscription examination were included in the study ($N = 717,963$). Among these women there were 41,910 *in situ* and 3,618 invasive cases of cervical cancer. Hazard ratios of *in situ* and invasive cervical cancer were estimated as functions of allergic rhinoconjunctivitis, asthma and eczema diagnoses in sons. Adjustment was made for the possible confounders: age, year of birth, education, socio-economic index, geography, number of conscripted sons and total number of offspring. The risk of *in situ* and invasive cervical cancer was lower for women having sons diagnosed with hypersensitivity (allergic rhinoconjunctivitis, asthma or eczema). Fully adjusted hazard ratios for women with 1 hypersensitive son were for *in situ* 0.86 (95% CI 0.84-0.88) and for invasive cervical cancer 0.82 (95% CI 0.74-0.91). The protective effects were similar between the 3 allergic diagnoses and increased with number of sons with a diagnosis. There was no significant association between non-cervical cancer in mothers and allergy in sons. These results strengthen the hypothesis that inherited immunological factors are important in determining risk of cervical cancer, probably by affecting mechanisms for viral persistence. © 2006 Wiley-Liss, Inc.

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Article Text

Cervical cancer is the second most common cancer among women worldwide, with 470,000 women diagnosed each year.[1] Infection with human papillomavirus (HPV) is considered a necessary but not sufficient cause of cervical cancer.[2] The reason why some women clear an HPV infection while others develop cervical lesions is still unknown. A key question is therefore what host and viral risk factors affect the persistence of infection and subsequent progression to cervical cancer?

Other environmental risk factors for cervical cancer are cigarette smoking, long-term use of oral contraceptives and high parity.[3][4][5] However, these factors do not explain why, once an HPV infection has occurred, some women progress to cervical cancer while others clear the virus.

The majority of studies on cervical neoplasias among immune-suppressed women suggest that impaired immunologic activity increases the risk of cervical cancer. Immune-suppressed individuals such as HIV patients or organ transplant recipients have increased risk for developing HPV-associated anogenital cancers.[6] Elevated risk of cervical cancer is reported for HIV/AIDS patients[7] and recipients of renal transplants.[8] An increased risk of cervical cytological abnormalities is seen in recipients of lung transplants[9] and bone marrow transplants.[10] These observations underline the importance of immunological response for development of cervical cancer.

Risk of cervical cancer appears to be influenced by inherited genes. An early observation by Goldgar *et al.* indicates increased risk of cervical cancer for first-degree relatives of probands and reports familial relative risk (FRR) of 1.74 (95% CI 0.86-2.91).[11] A twin study investigating familial cancer risk describes a heritable component for *in situ* cervical cancer.[12] Hemminki *et al.* present familial risks of similar magnitude for invasive and *in situ* cervical cancer but do not distinguish between environmental and genetic factors.[13] Magnusson *et al.* prove a doubled risk for biological first-degree relatives of cervical cancer cases whereas no increased risk was seen for non-biological first-degree relatives of cases, and results imply that the familial clustering to a large extent is due to genetic rather than environmental factors.[14] Further analysis reveals that heritability explains 27% of the variation in liability to disease (95% CI 26-29%). Sister-specific shared environment explains 2% (95% CI 1-4%) of the variance but shared environment between mother and daughter does not seem important.[15] Another study confirms the results for invasive cervical cancer with an estimated heritability of 22% (95% CI 14-27%) and 3% (95% CI 0-8%) of the variance attributable to shared childhood environment. For *in situ* cervical cancer the same study found a heritability of 13% (95% CI 6-15%), similar in magnitude to the shared childhood environment component, which was estimated to 13% (95% CI 12-24%).[16] Recent work on family history as a co-factor for cervical cancer supports the importance of host factors, although environmental effects cannot be ruled out.[17]

Allergy is a state of hypersensitivity caused by an immunological reaction towards a particular antigen, the allergen. Common symptoms of allergy are allergic rhinoconjunctivitis, asthma and eczema. There is strong

familial influence in the development of allergy and children with both parents being allergic have 50% risk of developing allergies. The reasons for this are genetic as well as environmental.[18]

The risk of developing cancer might be affected by variation in immunological status and activity; this would be particularly relevant for virally induced tumors. It is plausible that an increased immunological activity would decrease the risk of persistent HPV infection and thereby the risk of cervical cancer. Another aspect is the theory of immunological surveillance that states that the immune system constantly monitors the body for genetically altered cells and removes tumor cells at an early stage.[19] If allergic individuals have increased immunologic activity and thereby a more efficient surveillance of viruses as well as tumor cells, this would reduce their risk of cancer. Several studies explore the relation between allergy and cancer. Vena *et al.* investigate the association between allergy-related illnesses and cancer and report a decreased overall risk of cancer for allergic individuals but point out that there is variation between cancer sites.[20] Other studies confirm that the association is complicated and differs between organ sites as well as between types of allergy.[21][22][23]

We hypothesize that inherited immunological factors influencing susceptibility to allergy also influence the ability to clear HPV infections. By investigating whether there is a cross-trait parent-offspring association between allergy in sons and cervical tumor in mothers this hypothesis is tested.

Material and methods

Study population

Women born in Sweden between 1932 and 1960 were identified in the Swedish Multi-Generation register (MGR). Further, all their recorded non-adopted offspring born before 1986 were identified. Sons were linked to the Swedish Military Service Conscription Register (MSCR) in which information on allergy diagnoses given during the medical part of military conscription examination is available. Diagnoses used for allergy among sons were for allergic rhinoconjunctivitis ICD-8/9, 477 and ICD-10, J30; for asthma ICD-8/9, 493 and ICD-10; J45 and for eczema ICD-8/9, 691 and ICD-10, L20. A joint diagnosis called hypersensitivity consisting of any of the 3 diagnoses was also created. Women with at least 1 son participating in a military conscription examination between 1968 and 2002 were selected for further analysis. By record linkage to the Swedish Cancer Register (SCR) information on *in situ* and invasive cervical cancer diagnoses, ICD-7: 171, occurring between 1958 and 2002 was added for the women. Information on socio-economic factors was obtained from the Population and Housing Censuses (PHC) 1970 and 1990, and the Longitudinal Database of Education, Income and Occupation (LOUISE) of 2001. For a small fraction of women lacking information in the PHC due to death or emigration before 1970 ($N = 2,280$, 0.3%) the socio-economic variables were set to missing.

Among the 1,448,646 women born 1932-60, 1,132,406 (78%) had offspring born before 1986. Out of these 717,963 (63%) had at least 1 son who underwent military conscription examination. This set of women constitutes the cohort on which all major analyses were performed.

Statistical analysis

In Cox regression models, hazard ratios of *in situ* and invasive cervical cancer were investigated as functions of allergy diagnosis recorded during military conscription examination at age 18 years, among sons. Results are presented with 95% confidence intervals. All statistical analysis was done in SAS version 8.2.

The time in study for each woman is handled as age in days from birth to either of the following: (i) cancer diagnosis, (ii) death, (iii) emigration or (iv) end of follow up (Dec 31, 2002), whichever occurred first. Secular trends over calendar time are handled by allowing for separate base-line hazards for each birth-year (analysis stratified in individual birth-years). Hazard ratios are controlled for the following possible confounders: age; secular trends (birth-year); highest educational level recorded 1970, 1990 or 2001 (7 levels: <9 years of primary school, 9 years of primary school, <3 years of secondary school, 3 years of secondary school, <3 years higher education, 3 years or more in higher education or information missing due to death or emigration before the first registration of educational achievement occurred); socio-economic index (SEI) (3 levels: white-collar worker, blue-collar worker and others (farmers, students, unknown etc)); geography (conscription examination centre: Kristianstad, Göteborg, Stockholm, Karlstad, Östersund or Boden. Examination centre is determined by proximity to place of residence, the centre recorded for the first son was used for the analysis); number of conscripted sons and total number of offspring (born before 1986) of each woman classified as 1, 2, 3, 4 and more than 4.

Graphic illustration of the association between cervical cancer and number of allergic sons was prepared by plotting adjusted probabilities of cervical cancer diagnosis over age. Adjustments for year of birth, education, SEI, geography, number of conscripted sons and total number of offspring were made by Cox regression.

Bias may arise when families of different size are mixed. This was investigated by performing the dose response analysis of increasing number of allergic sons on a subset restricted to families with 2 conscripted sons. The number of women having exactly 2 conscripted sons were 188,723, among these were 10,946 *in situ* and 986 invasive cervical cancer cases. To reflect confounding of SEI and birth cohort stratified analysis of the risk of cervical cancer for women with at least 1 son diagnosed with hypersensitivity was performed. The stratifications were for SEI white-collar workers or blue-collar workers and for birth cohorts 1932-40, 1941-45, 1946-50, 1951-55 or 1956-60.

Association between non-cervical cancers (*i.e.* cancers occurring at sites other than the uterine cervix) among the mothers and hypersensitivity in conscription-examined sons was assessed in similar Cox regression models. All registered tumor diagnoses aside from ICD7: 171 were considered non-cervical.

Results

Among the 717,963 eligible women 41,910 were diagnosed with *in situ* cervical cancer and 3,618 were diagnosed with invasive cervical cancer during the follow-up time. The 2 major groups of excluded women were women without offspring and women with no conscription-examined son. Women excluded because they had no offspring were less likely to have developed *in situ* as well as invasive cervical cancer, in comparison to women with offspring. The hazard ratios adjusted for age, year of birth, education and SEI for women without offspring were 0.74 (0.72-0.75) for *in situ* and 0.77 (0.72-0.83) for invasive cancer. Rate of cervical cancer among women having offspring but excluded because they had no conscription-examined son did not differ from included women; hazard ratios adjusted for age, year of birth, education and SEI for women lacking conscripted son were 1 (0.98-1.02) for *in situ* cervical cancer and 1 (0.95-1.06) for invasive cervical cancer.

In situ cervical cancer

Results from the Cox regression analysis of *in situ* cervical cancer are shown in Table I. There was a protective effect of having sons diagnosed with allergic rhinoconjunctivitis, asthma or eczema. This was significant both in the simple model only adjusting for age and number of conscripted sons and in the model adjusting for age, year of birth, education, SEI, geography, number of conscripted sons and total number of

offspring. Fully adjusted hazard ratios were for women with 1 or more sons diagnosed with allergic rhinoconjunctivitis 0.84 (0.81-0.86), asthma 0.90 (0.86-0.94) and eczema 0.89 (0.83-0.94). The fully adjusted hazard ratios were slightly lower than or similar to hazard ratios adjusted only for age and number of conscripted sons.

Table I. Hazard Ratios for *In Situ* Cervical Cancer by Hypersensitivity in Sons

Type of hypersensitivity in son	<i>Nin situ</i> cervical cancer/N women	HR adjusted for age and number of conscripted sons (95% CI)	Fully adjusted HR (95% CI) ¹	<i>p</i> -value (fully adjusted model)
No son with allergic rhinoconjunctivitis	38,004/642,676	1	1	
1 or more son with allergic rhinoconjunctivitis	3,906/75,287	0.90 (0.88-0.94)	0.84 (0.81-0.86)	<0.0001
No son with asthma	39,493/673,225	1	1	
1 or more son with asthma	2,417/44,738	0.93 (0.90-0.97)	0.90 (0.86-0.94)	<0.0001
No son with eczema	40,979/699,769	1	1	
1 or more son with eczema	931/18,194	0.88 (0.83-0.94)	0.89 (0.83-0.94)	<0.0005
No son with hypersensitivity ²	35,685/599,753	1	1	
1 son with hypersensitivity	5,902/110,936	0.92 (0.89-0.94)	0.86 (0.84-0.88)	<0.0001
2 sons with hypersensitivity	320/7,015	0.78 (0.70-0.88)	0.73 (0.66-0.82)	<0.0001
>2 sons with hypersensitivity	3/259	0.20 (0.07-0.62)	0.17 (0.06-0.53)	<0.005

Adjusted for age, year of birth, education, SEI, geography, number of conscripted sons and total number of offspring.

² Any type (allergic rhinoconjunctivitis, asthma or eczema).

The combined diagnosis called hypersensitivity, including allergic rhinoconjunctivitis, asthma and eczema,

was also analyzed. The protective effect increased with number of sons diagnosed with hypersensitivity as shown in Table I. Fully adjusted hazard ratios were for women with 1 son diagnosed with hypersensitivity 0.86 (0.84-0.88), for women with 2 sons diagnosed with hypersensitivity 0.73 (0.66-0.82) and for women with more than 2 sons diagnosed with hypersensitivity 0.17 (0.06-0.53). Each of these estimates differs significantly from one and from each other (non-overlapping confidence intervals). The protective effect is illustrated by time-to-event functions plotted for women with no, 1 and more than 1 son with hypersensitivity, respectively, in Figure 1. In summary, the allergy diagnoses allergic rhinoconjunctivitis, asthma and eczema in sons were associated with reduced risk of *in situ* cervical cancer in mothers.

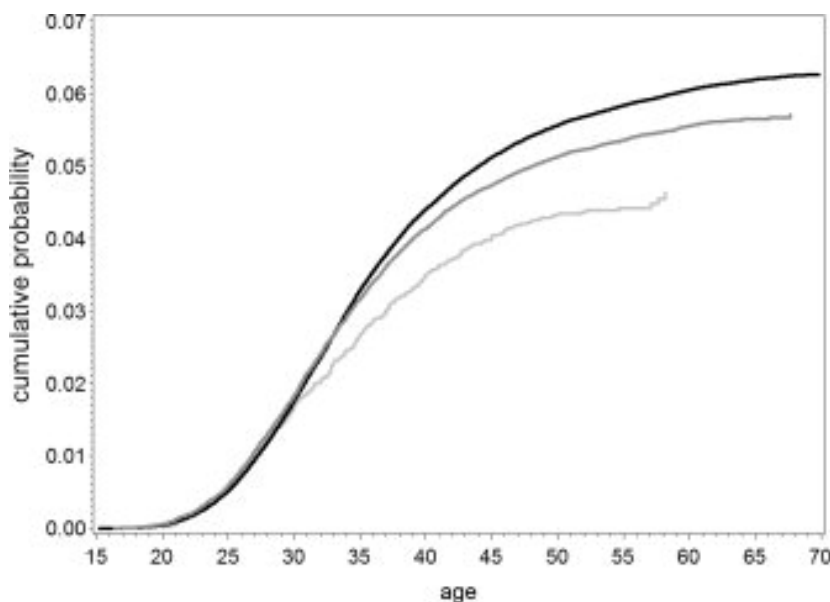


Figure 1. Time-to-event plot describing the probability of *in situ* cervical cancer over age in mothers with no (black curve), 1 (dark grey curve) and more than 1 (light grey curve) son diagnosed with hypersensitivity at conscription examination. The y-axis displays cumulative probability of *in situ* cancer diagnosis and the x-axis displays time as age in years. The probability curves are adjusted for year of birth, education, SEI, geography, number of conscripted sons and total number of offspring. - [Normal View 13K | Magnified View 34K]

Invasive cervical cancer

Invasive cervical cancer showed similar inverse relation with allergy in sons as observed for *in situ* cervical cancer. This is demonstrated in Table II. The fully adjusted hazard ratios were for women with at least 1 son diagnosed with allergic rhinoconjunctivitis 0.80 (0.71-0.92), asthma 0.80 (0.69-0.94) and eczema 0.79 (0.62-1.01). For allergic rhinoconjunctivitis and asthma, protective effects were significant for both models. For eczema the effects were similar in both models but not significant in the fully adjusted model.

Table II. Hazard Ratios for Invasive Cervical Cancer by Hypersensitivity in Sons

Type of hypersensitivity in son	N invasive cervical cancer/N women	HR adjusted for age and number of conscripted sons (95% CI)	Fully adjusted HR (95% CI) ¹	p-value (fully adjusted model)
No son with allergic rhinoconjunctivitis	3,355/642,676	1	1	

1 or more sons with allergic rhinoconjunctivitis	263/75,287	0.75 (0.66-0.85)	0.80 (0.71-0.92)	<0.001
No son with asthma	3,443/673,225	1	1	
1 or more sons with asthma	175/44,738	0.79 (0.68-0.92)	0.80 (0.69-0.94)	<0.01
No son with eczema	3,551/699,769	1	1	
1 or more sons with eczema	67/18,194	0.75 (0.59-0.96)	0.79 (0.62-1.01)	NS
No son with hypersensitivity ²	3,178/599,753	1	1	
1 son with hypersensitivity	423/110,936	0.78 (0.71-0.87)	0.82 (0.74-0.91)	<0.0001
2 sons with hypersensitivity	16/7,015	0.44 (0.27-0.72)	0.50 (0.30-0.82)	<0.01
>2 sons with hypersensitivity	1/259	0.68 (0.10-4.82)	0.71 (0.10-5.08)	NS

¹ Adjusted for age, year of birth, education, SEI, geography, number of conscripted sons and total number of offspring.

² Any type (allergic rhinoconjunctivitis, asthma or eczema).

Analysis of the joint diagnosis hypersensitivity revealed that risk of invasive cervical cancer was inversely correlated with the number of sons diagnosed with hypersensitivity, analogous with the findings for *in situ* cancer. The fully adjusted hazard ratios for women with 1 and 2 sons diagnosed with hypersensitivity were 0.82 (0.74-0.91) and 0.50 (0.30-0.82), respectively. Among mothers having more than 2 sons diagnosed with hypersensitivity the association was not significant; however, only 1 invasive cervical cancer diagnosis occurred among these women. The increase in protective effect in mothers by number of sons diagnosed with hypersensitivity is demonstrated as a time-to-event plot in Figure 2. In summary, having sons diagnosed with allergic rhinoconjunctivitis, asthma or eczema was associated with reduced risk of invasive cervical cancer in mothers.

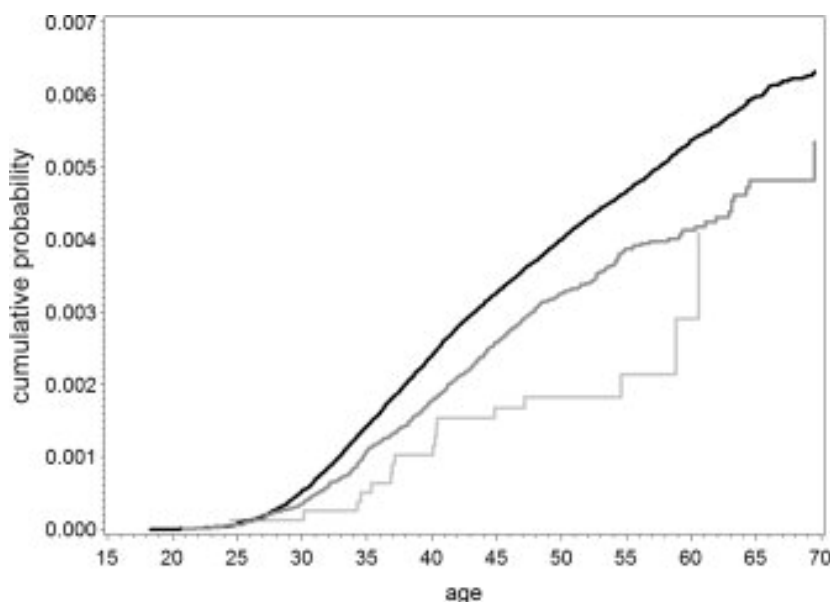


Figure 2. Time-to-event plot describing the probability of invasive cervical cancer over age in mothers with no (black curve), 1 (dark grey curve) and more than 1 (light grey curve) son diagnosed with hypersensitivity at conscription examination. The y-axis displays cumulative probability of invasive cancer diagnosis and the x-axis displays time as age in years. The probability curves are adjusted for year of birth, education, SEI, geography, number of conscripted sons and total number of offspring. [\[Normal View 15K | Magnified View 36K\]](#)

Confounding effects

The dose response analysis was also performed including only the 188,723 women having exactly 2 conscripted sons. Within this selected stratum of women the hazard ratios for *in situ* cervical cancer in the fully adjusted model were 0.88 (0.84-0.93) for women with 1 and 0.72 (0.64-0.82) for women with both sons allergic, with none of the sons allergic used as reference. These estimates are highly similar to what was observed in the full material. For invasive cervical cancer the fully adjusted hazard ratios were 0.87 (0.72-1.04) for women with 1 and 0.44 (0.23-0.82) for women with both sons allergic and no sons allergic used as reference. These estimates are similar to estimates obtained from the full material although the reduced number of cases resulted in slightly wider confidence intervals.

Results from the analysis of the different SEI and birth cohort strata are shown in Table III. There was no obvious effect of SEI stratification on *in situ* cervical cancer. Fully adjusted hazard ratios for women having at least 1 son diagnosed with hypersensitivity were 0.84 (0.80-0.87) for white-collar workers and 0.85 (0.82-0.89) for blue-collar workers. For invasive cervical cancer the corresponding hazard ratio was 0.80 (0.69-0.94) for white-collar workers and 0.76 (0.64-0.90) for blue-collar workers. Thus, the effect of having sons diagnosed with hypersensitivity was slightly more pronounced in blue-collar workers but the confidence intervals overlap and the protective effect was clearly visible in both strata.

Table III. Hazard Ratios of Cervical Cancer for Women Having One or More Sons with Hypersensitivity¹, Stratified by SEI and Birth-Cohort

	<i>In situ</i>	Invasive

Stratum	<i>N</i> women	<i>N</i> in situ cervical cancer	Fully adjusted HR (95% CI) ²	<i>p</i> -value	<i>N</i> invasive cervical cancer	Fully adjusted HR (95% CI) ²	<i>p</i> - value
SEI							
White collar workers	365,463	20,274	0.84 (0.80-0.87)	<0.0001	1,510	0.80 (0.69-0.94)	<0.01
Blue collar workers	275,404	17,269	0.85 (0.82-0.89)	<0.0001	1,428	0.76 (0.64-0.90)	<0.005
Birth cohort							
1932-1940	216,411	10,675	0.83 (0.77-0.90)	<0.0001	1,423	0.92 (0.74-1.14)	NS
1941-1945	161,940	10,185	0.81 (0.76-0.86)	<0.0001	784	0.71 (0.56-0.89)	<0.005
1946-1950	165,400	10,547	0.83 (0.79-0.88)	<0.0001	722	0.78 (0.64-0.95)	<0.05
1951-1955	117,248	7,125	0.91 (0.86-0.97)	<0.005	461	0.75 (0.60-0.95)	<0.05
1956-1960	56,964	3,378	0.92 (0.85-1.00)	NS	228	0.92 (0.67-1.26)	NS

¹ Any type (allergic rhinoconjunctivitis, asthma or eczema).

² SEI stratified analyses adjusted for age, year of birth, geography, number of conscripted sons and total number of offspring. Birth-cohort adjusted stratified adjusted for age, education, SEI, geography, number of conscripted sons and total number of offspring.

The results from the birth cohort stratification for *in situ* cervical cancer were quite consistent for the 3 oldest cohorts but the effect seemed less pronounced in the younger cohorts. The fully adjusted hazard ratios for women with at least 1 son diagnosed with hypersensitivity were for women born 1932-40, 0.83 (0.77-0.90); 1941-45, 0.81 (0.76-0.86); 1946-50, 0.83 (0.79-0.88); 1951-55, 0.91 (0.86-0.97) and 1956-60, 0.92 (0.85-1). For invasive cervical cancer the effect seemed stronger in the middle cohorts, and it was not significant for the oldest and the youngest cohort. However, all birth cohorts had point estimates showing a protective effect of having sons diagnosed with hypersensitivity. Fully adjusted hazard ratios of invasive cervical cancer for women in the different birth cohorts with at least 1 hypersensitive son were 1932-40, 0.92 (0.74-1.14); 1941-45, 0.71 (0.56-0.89); 1946-50, 0.78 (0.64-0.95); 1951-55, 0.75 (0.60-0.95) and 1956-60, 0.92 (0.67-1.26).

In summary, the reduced risk of cervical cancer associated with sons diagnosed with hypersensitivity was seen

when analysis was restricted to women having exactly 2 conscripted sons as well as in all cohorts when data was stratified for SEI or year of birth. Hence, it seems that the protective effect is present in all examined strata and not due to confounding caused by family size, SEI or birth cohort.

Specificity of effect

To investigate whether the observed associations reflected some mechanism general to all cancers, the association between all cancers other than cancer of the uterine cervix (non-cervical cancer) in mothers and allergy among sons was evaluated. No significant association was seen between non-cervical cancers in mothers and allergic rhinoconjunctivitis, asthma or eczema among sons. Fully adjusted hazard ratios for non-cervical cancers were for women with 1 or more sons diagnosed with allergic rhinoconjunctivitis 0.97 (0.94-1), asthma 0.98 (0.95-1.01) and eczema 0.97 (0.92-1.02). The observed protective effect is thus stronger for cervical than for non-cervical cancer.

Discussion

The results of this study reveal a cross-trait parent-offspring association between cervical cancer and allergy; having sons diagnosed with allergic rhinoconjunctivitis, asthma or eczema decreases the risk of *in situ* and invasive cervical cancer in mothers. The individual effects of the different diagnoses allergic rhinoconjunctivitis, asthma and eczema on the risk of *in situ* and invasive cancer were similar in magnitude, albeit the association between eczema and invasive cancer did not reach statistical significance.

The current study benefits from a very large sample size, long follow-up time and possibility to adjust for a number of potential confounding variables. The large number of subjects included in the study provides sufficient statistical power to detect also weak associations. We are not aware of any larger study exploring the connection between cervical cancer and allergy or of any other study investigating the influence of hereditary components shared between allergy and cervical cancer.

A drawback is that the study includes only male offspring, which means that the results are not necessarily valid for allergy among female offspring. However, there is no obvious reason why the observed effects should be limited to sons only. Another limitation is that the allergy diagnoses include atopic as well as non-atopic cases, which, in case the effect specifically reflects atopy, will lead to deflated estimates.

Our results are consistent with the findings of Vena *et al.* who studied 1,430 cervical cancer cases and report a strong inverse association between allergy and cancer of the cervix as well as an overall decrease in cancer risk associated with allergy. The age- and smoking-adjusted relative risk of cervical cancer associated with an allergy-related condition was 0.76 ($p < 0.05$).[\[20\]](#) Later studies of the association between cancer and allergies show differing results. Mills *et al.* conclude that the association between allergy and cancer depends on type of allergy and varies between organ sites but is not significant for the cervix.[\[21\]](#) Källén *et al.* demonstrate a reduction of overall cancer incidence in asthmatic subjects with an observed cancer rate that is two thirds of the expected, but point out that the effect differs between cancer types. The uterine cervix is among the sites showing a protective effect with 52% of the expected cases (95% CI, 38.9-69.1).[\[22\]](#) Vesterinen *et al.* show increased as well as decreased cancer risks in asthmatic patients and note a non-significant protective tendency for cervical cancer.[\[23\]](#)

Allergy and cervical cancer are complex traits and the observed familial association may well reflect both genetic and environmental factors. The current study design does not allow deductions regarding the relative impact of the different factors. However, previous investigations of heritability suggest that the major part of

the familial aggregation in cervical cancer is due to genetics.[15][16] A Finnish twin study reports 74-82% heritability for allergic rhinoconjunctivitis (hay fever), previous estimates vary between 33 and 70%,[24] and a review of twin studies on asthma lists heritability estimates ranging from 36 to 79%.[25] High heritability is also reported for eczema (atopic dermatitis).[26] Taken together, this supports that the observed cross trait, parent offspring association to a large extent is explained by genetic factors.

Human leukocyte antigen (HLA) molecules are essential for clearance of viral infections and established candidate genes for involvement in cervical cancer development. An affected sib-pair study demonstrates excess genetic sharing for the HLA class II loci DPB1, DQB1 and DRB1[27] and various loci in the HLA region have been associated with cervical cancer.[28] Interestingly, DQB1*0602, the cervical cancer risk allele, is reported as a protective factor in allergic rhinitis[29] while DQB1*0603, that reduces risk of cervical cancer, is suggested to increase the risk of occupational asthma.[30] Both findings support the idea of an inverse relation between susceptibility to cervical cancer and allergy. HLA alleles show association with many different traits and allele frequencies differ between populations. Still, it appears likely that some of the hereditary influence detected in our study is due to genetic variation within the HLA locus.

In conclusion, we found that allergy in sons is associated with decreased risk of cervical cancer in their mothers. This supports the hypothesis that inherited immunological factors are important for susceptibility to cervical cancer, probably by influencing the likelihood of clearance versus persistence of HPV infection. This may have implications for ongoing development of vaccines against cervical cancer.

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