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Cancer risk among Danish and Italian farmers

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Abstract

Cancer risk for farmers in Denmark and Italy was studied by linking occupational census data with incidence of cancer in Denmark and with cancer mortality in Italy. Farmers in the two countries had a consistent risk reduction for cancer of the lung, bladder, small intestine, colon, rectum, and prostate. No excess of stomach cancer was found among farmers in the two countries, which is in agreement with the most recent data from other surveys. The risk of oesophageal cancer was reduced among the Danish and increased among the Italian male farmers. This can probably be explained by differences in alcohol consumption between the Danish and Italian farmers compared with the general population. The risk of brain cancer was significantly reduced among Italian farmers. There was a significant risk reduction for Hodgkin's disease and no excess for non-Hodgkin's lymphoma in Denmark, whereas in Italy a statistically significant excess risk was found for the first and a slight excess risk for the second of these diseases. The per capita consumption of phenoxy-herbicides between 1950 and 1970 was lower in Italy than in Denmark but treatments were performed mainly by professional applicators in Denmark and by the farmers themselves in Italy. Risk of leukaemia among Italian female farmers was increased. In Denmark, this increase was limited to women who were themselves owners of a farm. Specific occupations in agriculture showing a high risk for cancers of the lymphopoietic system in Denmark mostly entailed contact with animals.

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Farmers are a group known to be at low overall risk of cancer and to have low overall mortality. The low risk of cancer is the result of a low frequency among farmers of the most common cancer sites, like lung cancer and colon cancer. An excess risk among farmers has, however, been reported for stomach cancer and for some, generally uncommon, cancer sites.

Findings from different countries are, however, conflicting and both the reasons for the deficits and the exposures responsible for the excesses are not understood. Moreover, reports are available only from a limited number of countries where surveillance systems based on routine records have been running for many years, such as North America, New Zealand, England and Wales, and Nordic Countries. Only a few studies on specific cancer sites among farmers in Southern Europe are available.

Recently Italian mortality data have been experimentally linked with census data to describe socioeconomic differentials in mortality. This has provided the opportunity of comparing the cancer risk among farmers in a Nordic country and in a Mediterranean country. Both the lifestyle of farmers and the agricultural activities show important differences between these countries and the comparison can thus provide further insight into the peculiar cancer risk profile of farmers.

Materials and methods

COHORTS AND CANCER CASES

A cohort of farmers of both sexes, 15 to 74 years old, was identified from the Danish Occupational Cancer Register for a 10 year follow up study of cancer incidence in the 1970 census population. Occupation was coded according to a special Danish nomenclature. For the present study two broad categories of farmers (self employed and employees) were considered for men and three (self employed, family workers, and employees) for women. A women was defined as a family worker if she was actively involved in the work of a farm owned by her husband. Detailed groups defined by specific occupations were also considered for cancers of the lymphopoietic system.

The cancer cases in the Danish cohort were identified through the record linkage between the

Table 1 Standardised incidence ratios (SIRs) and mortality odds ratios (MORs) of cancer among male Danish and Italian farmers

	Denmark					*Italy*					
	Self employed		*Employees*			*Self employed*			*Employees*		
Cancer sites	*Obs*	*SIR*	*Obs*	*SIR*		*Obs*	*MOR*	*Adjusted MOR*	*Obs*	*MOR*	*Adjusted MOR*
Lip	182	1·80*	43	2·09*							
Tongue	9	0·58	2	0·63							
Salivary glands	13	0·92	0	0·00		13	1·14	0·91	4	0·62	0·50
Mouth	14	0·47*	0	0·00*							
Pharynx	13	0·32*	9	1·10							
Oesophagus	32	0·44*	13	0·92		15	1·81*	1·45	5	1·08	0·86
Stomach	286	0·94	71	1·21		66	1·25	1·00	34	1·42	1·14
Small intestine	12	0·58	1	0·24	†	6	0·51	0·41*	2	0·39	0·31
Colon	277	0·70*	45	0·58*							
Rectum	309	0·83*	55	0·77*		29	0·93	0·74	7	0·46*	0·37*
Liver	23	0·37*	9	0·75							
Gallbladder	35	0·76	7	0·78		28	0·86	0·69	10	0·67	0·54
Liver not specified as primary	13	0·85	3	1·00							
Pancreas	137	0·64*	23	0·55*		29	1·34	1·07	12	1·17	0·94
Peritoneum and unspecified digestive	18	1·22	3	0·92	‡	—	—	—	—	—	—
Nasal cavities and sinuses	11	0·58	5	1·27		0	0	0·00	1	4·15	3·32
Larynx	38	0·29*	12	0·47*		13	1·07	0·86	4	0·69	0·55
Lung	559	0·40*	191	0·72*		111	0·64*	0·51*	67	0·84	0·67*
Pleura	10	0·37*	3	0·57		4	1·47	1·18	0	0	0·00
Lung not specified as primary	5	0·41*	0	0·00		—	—	—	—	—	—
Mediastinum and unspecified respiratory	0	0·00*	0	0·00		5	1·81	1·45	0	0	0·00
Breast	5	0·48	3	1·37		—	—	—	—	—	—
Prostate	399	0·89*	63	0·76*		10	0·9	0·72	2	0·53	0·42
Testis	74	0·93	23	0·64*		—	—	—	—	—	—
Other and unspecified genital	16	0·73	4	0·89		—	—	—	—	—	—
Kidney	141	0·64*	18	0·41*		14	1·46	1·17	2	4·88	3·90
Bladder	300	0·55*	70	0·65*		12	0·81	0·65	2	0·34	0·27
Melanoma of skin	72	0·67*	17	0·64		6	1·43	1·14	0	0	0·00
Other skin	493	0·69*	98	0·69*		—	—	—	—	—	—
Eye	19	0·91	6	1·34		—	—	—	—	—	—
Brain and nervous system	194	1·06	39	0·93	§	13	0·69	0·55*	7	0·71	0·57
Thyroid	13	0·70	5	1·13		—	—	—	—	—	—
Endocrine glands	8	0·83	1	0·45		—	—	—	—	—	—
Bone	9	0·92	2	0·64		—	—	—	—	—	—
Connective tissue	27	1·21	5	0·93		—	—	—	—	—	—
Metastases	60	0·71*	24	1·43		—	—	—	—	—	—
Other and unspecified sites	29	0·95	8	1·33		—	—	—	—	—	—
Non-Hodgkin's lymphoma	120	1·01	27	1·02	‖	9	1·59	1·27	5	1·67	1·34
Hodgkin's disease	27	0·63*	13	1·01		10	2·91*	2·33*	1	0·41	0·33
Multiple myeloma	63	0·96	20	1·57*		1	0·31	0·25	0	0	0·00
Leukaemia	145	0·92	33	0·98		12	0·81	0·65	8	1·09	0·87
Mycosis fungoides	4	0·82	0	0·00	¶	—	—	—	—	—	—

Adjusted MOR = Mortality odds ratios adjusted to allow for the low general mortality of farmers (see materials and methods).
*$p < 0·05$.
†Includes peritoneum and unspecified digestive.
‡Included in small intestine.
§Includes malignant and benign tumours of the nervous system (ICD–9: 191, 192, 225, 237·5, 237·9, 239·6).
‖Includes mycosis fungoides.
¶Included in non-Hodgkin's lymphoma.
Obs = No of observed cases.

1970 census data and the Danish Cancer Register. Cancer sites, coded according to the International Classification of Diseases, seventh revision (ICD–7) (1970–1977) and ICD–0 (1978–1980), were assembled in 47 standard diagnostic groups.[1]

In the Italian study a cohort of farmers of both sexes aged 18 to 74 years was identified from the 1981 census and the mortality was followed up for six months (11 November 1981 to 11 April 1982). Job title and economic activity were coded according to the Italian classifications.[2,3] For the present study two job titles were considered: self-employed farmers (code 3.1) and employees (codes 3.2 and 3.3). The Italian classification of occupations does not include a title for family workers in agriculture and criteria for defining self employed farmers among women were not strict.

Cancer deaths in the Italian cohort were identified through record linkage between death certificates and the 1981 census data. The linkage key was provided by the local population registries where the death occurred. Cooperation was provided by 96% of the registries (90% of the deaths). The proportion of non-linked deaths was 16% resulting in an overall 75% (90% × 84%) of successful matching. Further details are described elsewhere.[4] Causes of death,

Table 2 Standardised incidence ratios (SIRs) and mortality odds ratios (MORs) of cancer among female Danish and Italian farmers

	Denmark							Italy					
	Self employed		Family worker		Employees			Self employed			Employees		
Cancer sites	Obs	SIR	Obs	SIR	Obs	SIR		Obs	MOR	Adjusted MOR	Obs	MOR	Adjusted MOR
Lip	0	0·00	0	0·00	0	0·00							
Tongue	0	0·00	0	0·00	0	0·00							
Salivary glands	0	0·00	4	1·11	1	3·33		0	0	0·00	0	0	0·00
Mouth	0	0·00	4	0·69	0	0·00							
Pharynx	0	0·00	5	0·90	0	0·00							
Oesophagus	1	1·35	2	0·36	0	0·00		0	0	0·00	0	0	0·00
Stomach	5	1·01	27	0·70	5	1·66		8	1·26	0·88	2	0·60	0·42
Small intestine	0	0·00	5	1·10	0	0·00	†	1	0·36	0·25	1	0·79	0·55
Colon	14	0·89	112	0·93	2	0·21*							
Rectum	5	0·56	55	0·80	2	0·38		6	0·89	0·62	1	0·31	0·22
Liver	0	0·00	5	0·54	0	0·00							
Gallbladder	7	2·66*	17	0·95	1	0·73		3	0·53	0·37	3	1·37	0·96
Liver not specified as primary	1	2·27	3	0·83	0	0·00							
Pancreas	7	1·20	27	0·66*	4	1·27		0	0	0·00	0	0	0·00
Peritoneum and unspecified digestive	1	2·13	5	1·15	0	0·00	‡	—	—	—	—	—	—
Nasal cavities and sinuses	1	3·45	0	0·00	0	0·00		0	0	0·00	0	0	0·00
Larynx	0	0·00	1	0·15*	0	0·00		0	0	0·00	0	0	0·00
Lung	3	0·24*	51	0·45*	6	0·68		5	0·91	0·64	5	2·12	1·48
Pleura	0	0·00	2	0·69	0	0·00		0	0	0·00	0	0	0·00
Lung not specified as primary	0	0·00	0	0·00	0	0·00		—	—	—	—	—	—
Mediastinum and unspecified respiratory	0	0·00	1	0·75	0	0·00		0	0	0·00	0	0	0·00
Breast	41	0·87	429	0·81*	25	0·60*		19	0·91	0·64	5	0·37*	0·26*
Cervix uteri	7	0·47*	100	0·50*	12	0·77							
Corpus uteri	8	0·56	103	0·82*	9	0·91		6	1·02	0·71	5	1·75	1·23
Uterus other and unspecified	0	0·00	0	0·00	0	0·00							
Ovary	12	0·90	104	0·78*	5	0·48		3	0·56	0·39	1	0·31	0·22
Other and unspecified genital	2	1·12	11	0·67	1	0·77		—	—	—	—	—	—
Kidney	4	0·90	30	0·78	3	1·00		1	0·86	0·60	2	4·23*	2·96
Bladder	1	0·19	25	0·61*	2	0·63		0	0	0·00	1	5·12	3·58
Melanoma of skin	5	1·17	32	0·56*	7	1·51		1	0·95	0·67	2	2·31	1·62
Other skin	5	0·31*	90	0·61*	10	0·86		—	—	—	—	—	—
Eye	0	0·00	8	1·87	0	0·00		—	—	—	—	—	—
Brain and nervous system	5	0·95	51	0·92	2	0·45	§	1	0·27	0·19	2	1·02	0·71
Thyroid	1	1·27	15	1·67*	1	1·35		—	—	—	—	—	—
Endocrine glands	0	0·00	2	0·84	0	0·00		—	—	—	—	—	—
Bone	0	0·00	1	0·56	1	6·25*		—	—	—	—	—	—
Connective tissue	0	0·00	5	0·96	1	2·38		—	—	—	—	—	—
Metastases	1	0·52	15	0·84	2	1·43		—	—	—	—	—	—
Other and unspecified sites	1	0·82	11	1·14	1	1·35		—	—	—	—	—	—
Non-Hodgkin's lymphoma	4	1·29	21	0·78	1	0·47	‖	1	0·92	0·64	2	3·28	2·30
Hodgkin's disease	1	1·11	9	0·92	1	1·22		1	1·87	1·31	0	0	0·00
Multiple myeloma	6	3·30*	16	1·32	0	0·00		1	1·50	1·05	0	0	0·00
Leukaemia	8	2·22*	27	0·89	3	1·25		5	1·71	1·20	4	2·22	1·55
Mycosis fungoides	0	0·00	0	0·00	0	0·00	¶	—	—	—	—	—	—

Adjusted MOR = Mortality odds ratios adjusted to allow for the low general mortality of farmers (see materials and methods).
*$p < 0·05$.
†Includes peritoneum and unspecified digestive.
‡Included in small intestine.
§Includes malignant and benign tumours of the nervous system (ICD–9: 191, 192, 225, 237·5, 237·9, 239·6).
‖Includes mycosis fungoides.
¶ Included in non-Hodgkin's lymphoma.
Obs = No of observed cases.

coded according to ICD–9, were grouped in 30 categories.

STATISTICAL ANALYSIS

For Danish data, the number of expected cancer cases was calculated by multiplying the person years at risk during the 10 year follow up period in each five year age group with the site specific incidence rates calculated in the same way for all persons economically active in 1970. The ratio between the total number of observed and the total number of expected cases is the standardised incidence ratio (SIR). Two sided χ^2 tests were performed assuming a Poisson distribution of observed cases.

For the Italian data, correct denominators were available only for the entire group of persons employed in agriculture, forestry, and fishing. Therefore, mortality odds ratios (MORs) were com-

puted for each cancer site, according to Mantel and Haenszel,[5] and adjusted for age in three groups (18–44, 45–64, 65–74). Subjects dying from all other causes of death were used as referents. Test based 95% confidence intervals (95% CIs) were computed according to Miettinen.[6] Moreover, to allow for the low overall mortality, we multiplied these MORs (95% CIs) with the ratio of overall mortality in agriculture, forestry, and fishing and overall mortality in all other branches (adjusted for the same age classes, 0·8 for men and 0·7 for women).

Results

EPITHELIAL CANCERS

Table 1 presents relative risk (RR) estimates (SIRs and MORs respectively) for each cancer site among Danish and Italian male farmers.

A reduced risk was found among both groups for cancers of the lung, bladder, small intestine, colon, rectum, and prostate (statistically significant in the Danish data and, for lung cancer, also in the Italian data). The reduction was greater among self employed farmers for lung cancer and among employees for cancer of colon and rectum. The RR of stomach cancer was also similar, near unity with a slight excess among employees, for both Italian and Danish farmers.

For brain cancer SIRs were also around unity in Danish data whereas the overall MOR for Italian male farmers was 0·54. The Italian result was statistically significant ($p < 0·05$).

Significant risk reductions were found among Danish men for cancers of the pancreas and larynx but not among the Italians.

In Denmark the SIR for oesophageal cancer among self employed male farmers was reduced. On the other hand, self employed Italian male farmers experienced an increased mortality from this cancer.

The situation was similar for women (table 2), taking into account that numbers were small for the Italians and with the exception of an increased risk (but based on five observed cases only) of lung cancer among Italian employees. Risk for breast cancer was reduced in both Italian and Danish farmers, the lowest risk being for employees.

The RR of cancer of the cervix and (to a smaller extent) corpus uteri, was less than unity for Danish farmers. The RR for cancer of the uterus was around one among Italian women.

CANCERS OF THE LYMPHOPOIETIC SYSTEM

A significant reduction in the risk of Hodgkin's disease among male self employed farmers emerged from the Danish data. On the other hand a significant excess was found among Italian self employed men.

A slight excess risk of non-Hodgkin's lymphoma was seen both in men and women in Italian data, although based, especially among women, on small numbers. No excess was found among Danish farmers in general, only for the small group of self employed women.

Danish data showed no excess of leukaemia among both men and women working in farms where the man is the farmer. In a few farms in which the owner is a woman, a high risk was found for women, although this result is based on eight cases only. Italian data are similar in that no excess was found among men but the risk was increased among women working in agriculture. In the Danish data the RR of multiple myeloma was near one for self employed men, there was a slight excess for male employees and female family workers, and a strong excess among self employed women. Italian data were uninformative, given the small number of cases.

Table 3 reports the specific occupations related to agriculture and showing an excess risk (observed > (expected + expected$^{1/2}$)) of cancers of the lymphopoietic system in Denmark. Many of them (self employed/special farms, tractor driver/agricultural services, cowman) entail animal handling. Self employed veterinarians were also at high risk of leukaemia and multiple myeloma. It is also interesting that, in Italy, the only two cases (one man and one woman) of myeloma were found in persons concerned with animal feeding despite the fact that a total of only 48 deaths occurred in this category among men and only five deaths among women.

Discussion

For epithelial cancers, the strongest difference bet-

Table 3 Specific occupations in agriculture showing an excess risk of lymphatic cancers in Denmark

	Obs	*SIR*
Men		
Non-Hodgkin's lymphoma:		
Farm worker living on farm	8	1·46
Cowman	6	3·02
Self employed/special farms	4	1·91
Self employed/large farms	4	2·46
Hodgkin's disease:		
Tractor driver/agricultural services	2	4·50
Multiple myeloma		
Gardener's labourer	6	2·48
Cowman	4	4·30
Leukaemia		
Self employed/ordinary farms	28	1·43
Self employed/special farms	5	1·82
Tractor driver/agricultural services	3	4·68
Women		
Multiple myeloma		
Family worker/ordinary farms	7	2·11
Leukaemia		
Family worker/gardening	5	2·47
Self-employed/ordinary farms	4	4·45

Obs = No of observed cases.

ween the two data sets concerns the risk of oesophageal cancer, which is reduced among Danish and increased among Italian male farmers. This last finding is at variance with the results of most reports from other countries where the risk of oesophageal cancer is generally reduced[7-12] or near one.[13-16] An exception is France where a higher incidence of oesophageal cancer among farmers has been reported.[17] Although in the past, in both countries, cigarette consumption has been lower among farmers than in the general population, alcohol consumption has been higher than the national average among Italian male farmers, at least in the recent past.[18] The difference in the risk of cancer of the larynx, another tobacco and alcohol related cancer (strongly reduced in Denmark and slightly reduced in Italy) and the excess risk for oesophageal cancer in France, where patterns of alcohol consumption are similar to the Italian ones, strengthen this interpretation.

Another major difference concerns the RR for brain cancer, which is around one among Danish farmers of both sexes and reduced among Italian men. This result is surprising because significantly[11 19] or non-significantly[7 12 14-16 20 21] increased risks of brain cancer have been reported by a number of studies on farmers. Moreover, an Italian hospital based case-control study[22] found a significantly increased risk of glioma among subjects reporting as having ever worked as farmers, especially among insecticide and fungicide users. The discrepancy may be explained by a diagnostic bias in Italian farmers, who make less use of advanced diagnostic aids for brain cancer. Such a bias could affect a study based on death certificates but not a case-control study, where both cases and controls were inpatients in specialised neurological institutions.

The risk of the remaining epithelial cancers is similar in the two countries and it is in general consistent with previous results, except for stomach and prostate cancer. A statistically significant positive association between farming and prostatic cancer was reported by some previous studies[7-9 11 12 15 19 23] although there was no consistent evidence about the responsible exposure.[24] Stomach cancer was traditionally associated with farming[24] although a number of surveys concerning more recent calendar years found no excess.[11 19 21 25 26] In southern Italy, where agriculture is by and large the most common activity, the incidence of stomach cancer is low,[27] possibly because of a high consumption of fresh fruits and vegetables.

Differences in the RR of Hodgkin's disease (significantly increased among Italian men only) and non-Hodgkin's lymphoma (increased in Italian but not in Danish farmers) are remarkable.

In a review of cancer risk among farmers[24] six studies out of 11 showed an excess risk of non-Hodgkin's lymphoma. Specific agricultural activities and characteristics have been linked to non-Hodgkin's lymphoma, like working in orchards,[19] chicken and pig production, and consumption of herbicides, insecticides, and fertilisers by county.[12] Case-control studies[28-31] found an association between non-Hodgkin's lymphoma and exposure to phenoxy herbicides although one study gave negative results[32] and another found an increased risk only in specific subgroups.[33] Although comparisons are difficult, the per capita consumption of phenoxy herbicides was much lower in Italy than in Denmark in the years between 1950 and 1970. It must, however, be considered that, in this period, treatments were performed mainly by professional applicators in Denmark and directly by farmers in Italy, and that the use of protective devices was low or absent in Italy. A high risk of soft tissue sarcoma, based on small numbers, was found in an Italian case-control study for female rice weeders occupied in 1950–5 and potentially exposed to phenoxy herbicide.[34]

Existing data support an association between farming and Hodgkin's disease (in Blair's review[24] six out of eight studies showed an RR above unity) but they do not provide clear cut evidence as to whether chemical or biological agents or both are involved.[24 35] Therefore it is difficult to interpret the difference between Italian and Danish findings. It is remarkable, however, that in mortality[36] and incidence[8] data from Sweden SMR was 0·98 and SIR was 1·04. Differences in agricultural characteristics, related both to climate and to a later introduction of modern farming techniques (including protective devices) in Italy could be involved. In some recent studies[12 21] the excess risk is concentrated in the older cohorts, suggesting that it is related to old agricultural activities.

Data on leukaemia from both countries are consistent in finding no excess risk among male farmers and an excess among self employed women; a similar pattern was found for multiple myeloma. Farms owned by women could have different characteristics and probably, in both countries, they more frequently manage activities like poultry and horse feeding. This would be consistent with results on specific activities at risk in Denmark, which often entail contact with animals, and with results on risk of myeloma in animal feeding in Italy. The virus of fowl leucosis was suggested as a possible agent of human leukaemia,[37] although the epidemiological evidence is contradictory,[24] and an association between chronic lymphatic leukaemia and contact with horses was reported in Sweden.[38] It must, however, be noted that Danish family workers, who frequently feed poultry, do not have an increased risk of leukaemia.

Comparing occupational disease or mortality data from different countries is not always straightforward. The classifications, the structure of the labour market, and the lifestyle associated with specific

occupations may differ. This exercise, which is a first attempt to analyse the Italian occupational mortality data, illustrates these problems.

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