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Cancer incidence on a small island – Research opportunities in general practice

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Objective **– To test the impression of an increased cancer incidence on the island of Pellworm (in the far North of Germany) and to illustrate the feasibility of a general practice-based approach in epidemiological research.**
Design **– Cancer incidence on Pellworm was prospectively registered in the only general practice on the island from 1986 to 1992. Age-standardized rates and expected rates were calculated on the basis of the Saarland cancer registry, the only registry in Germany. Standardized incidence ratios and 95% confidence intervals (CI) for Poisson-distributed events were also calculated. The cancer data were summed up over a seven-year period.**
Setting **– The only general practice on the island of Pellworm, a North Frisian marshland-island.**
Subjects **– The total practice population between 1986 and 1992 (N = 1 172)**
Results **– The crude annual cancer incidence rate for Pellworm was, according to the impression, unexpectedly high: 634/100 000 for men and 502/100 000 for women. After age standardization, however, this increased rate of cancer incidence was even lower than in the Saarland (ratios: 0.86 for men and 0.95 for women). Only the incidence of neoplasms of the lymphatic and haematopoietic tissue in men exceeded the limits of statistical likelihood (ratio: 3.21; 95% CI: 1.17–7.10).**
Conclusion **– The impression of an increased rate of cancer on Pellworm could not be validated. The overall incidence rate was even lower than expected. Only the rate of leukaemia/lymphoma (men) was significantly higher. Reasons for this result could not be detected by a descriptive approach. General practice is a suitable place for studies in cancer epidemiology, especially in such ideal circumstances as a clearly limited area and complete and reliable documentation.**

Key words: **family practice, neoplasms – epidemiology, registries – standards.**

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"Now she too is dying. It's the curse of these marshes, cancer, that has got her" – this is a statement of one of the characters in Theodor Storm's novel "The White Horse Rider" (1). Storm, a well-known North Frisian poet, suffered himself from cancer of the stomach and died in

1888. The literary assumption of a coincidence between cancer and the mud flats landscape was never scientifically discussed and would be rather unlikely because most studies in this field report lower cancer rates in rural than urban populations (2–4). Yet one of the authors (UK), who runs the only (general) practice on the island of Pellworm, was reminded of Theodor Storm's novel when he saw many cancer patients in his practice population. This impression was supported by the fact that in some areas of the island nearly all houses seemed to have or to have had a cancer patient. The impulse for this study was to validate this impression by calculating age-standardized incidence rates for comparison with a suitable cancer registry.

Methods

Pellworm, one of the North Frisian islands in the North Sea, is a mud flats island of 14.3 square miles. Fertile clay-lands are the basis for agriculture. Parts of the island are up to 3 yards below sea level so that sewers run through the island for draining. Until 1965 water was obtained from hollows, wells, or rainwater. Now a water pipe connects the island with the mainland. Today the island has a population of 1 100 (77 inhabitants/square mile). Most of the islanders work in agriculture or for tourism. The economic conditions (wages, rate of unemployment) are worse than on the mainland: the average income is above 40% lower than for the rest of Germany (West).

The study refers to the data from the only surgery on the island run by two general practitioners. All cancer patients of the practice were systematically registered since 1986. Cancers were classified according to the 9th International Classification of Diseases (ICD–9) (5). Further details of this registry include age and sex of the patients and investigations performed to reach the diagnosis of cancer.

As the crude cancer rates suggested a high incidence of cancer on Pellworm, a cancer register was needed for valid comparision. The Saarland registry was chosen because it is the most reliable cancer registry in Germany (West), and reliable cancer incidence rates have been recorded during the last two decades (6). The Saarland is one of the smallest federal states of Germany with 1.05 million inhibitants and a population density of 157 persons/square mile, which corresponds to the "small urban" category (4).

To compare the data, age standardized incidence rates and expected rates for Pellworm were calculated on the basis of the age distribution of the population of the Saarland. For this purpose computer-assisted programmes were used (at the Federal Institute for Radiation Safety [Bundesanstalt für Strahlensicherheit] (7) and at the Institute of Epidemiology of the Federal Health Administration [Bundesgesundheitsamt]) (8). Standardized incidence ratios were calculated by using the formula observed cases (standardized): expected cases (standardized). Additional to this point estimate, 95% confidence intervals (CI) were determined for the true standardized incidence ratio using exact intervals for Poisson-distributed events according to Fisher. If 1.0 is not included by the CI, the true incidence rate for cancer is (with 95% likelihood) higher or lower than expected.

Rates and CIs were calculated for each year, but to cope with the variability in annual incidence of cancer rates for small populations, only totals over the whole observation period of 7 years are reported.

Results

From 1986 to 1992, 1 172 patients living on Pellworm (representing nearly 100% of the population) had at least one appointment at the surgery. For each person who died in this period the death certificate was issued by one of the two doctors of the practice.

In the seven year period 45 persons, 24 (53%) of them male, were registered because of a new episode of cancer (Table I). Their mean age was 67.8 (men) and 66.1 years (women). The diagnosis was validated histologically or cytologically in all but 3 cases.

On average, the crude annual cancer incidence rate for Pellworm was 634/100 000 for men and 502/100 000 for women and thus far higher than the incidence rate for the Saarland (483 and 310, respectively). The age-standardized incidence ratio, however, showed no excess, but even fewer cases of cancer than expected: 0.86 for men and 0.95 for women (Table II). This relatively low

Table I. Cancer registry for Pellworm.

Calendar year	Diagnosis	ICD	Sex	Age	Verification*
1986	Chronic myeloid leukaemia	205	M	61	hist
	non-Hodgkin's lymphoma	200	F	72	hist
	non Hodgkin MALT	202	M	61	hist
1987	Breast	174	F	39	hist
	Bronchus	162	M	82	cyto
	Rectum	154	M	66	hist
	Colon	153	F	65	hist
	Acute lymphoid leukaemia	204	M	17	hist
	Cervix uteri	180	F	28	hist
	Pancreas	157	F	74	cyto
	Breast	174	F	69	hist
	Breast	174	F	75	hist
1988	Bronchus	162	F	74	hist
	Bronchus	162	M	76	cyto
	Rectum	154	M	80	hist
	Chronic myeloid leukaemia	205	F	70	cyto
	Chronic lymphoid leukaemia	204	M	73	cyto
1989	Bronchus	162	M	76	hist
	Bronchus	162	M	75	hist
	Stomach	151	M	65	hist
	Renal carcinoma	189	M	64	hist
	Colon	153	F	76	hist
	Chronic lymphoid leukaemia	204	M	65	cyto
1990	Breast	174	F	45	hist
	Stromach	151	M	69	hist
	Rectum	154	M	58	hist
	Pancreas	157	M	71	cyto
	Corpus uteri	182	F	72	hist
1991	Bronchus	162	M	68	hist
	Prostate	185	M	69	hist
	Colon	153	M	63	clin
	Pharynx	149	M	54	hist
	Melanoma	172	F	71	hist
1992	Breast	174	F	79	hist
	Breast	174	F	65	hist
	Breast	174	F	66	hist
	Pleura	163	M	62	hist
	Bronchus	162	M	67	hist
	Prostate	185	M	70	hist
	Rectum	154	F	83	hist
	Sarcoma of the uterus	182	F	56	hist
	Larynx	161	M	64	hist
	Colon	195	F	73	clin
	Corpus uteri	182	F	86	clin

* Verification by histological (hist), cytological (cyto) or clinical (clin) examination

Table II. Observed and expected cancer incidences; 1986–1992.

Cancer site (ICD)	Cases		SIR*	95% CI**
	observed	expected		
Mouth, lip, pharynx (140–149)				
– male	1	1.17	0.85	0.04–4.22
– female	0	0.23	–	–
Digestive organs (150–159)				
– male	7	8.33	0.84	0.37–1.66
– female	4	7.36	0.54	0.17–1.13
Respiratory organs (160–165)				
– male	8	7.37	1.09	0.50–2.06
– female	2	1.05	1.90	0.32–6.29
Melanoma (172)				
– male	0	0.35	–	–
– female	1	0.35	2.86	0.14–14.09
Breast (174)	7	4.99	1.40	0.61–2.78
Female genitourinary organs (179–184)	4	3.50	1.14	0.36–2.76
Prostate and testis (185–186)	2	2.45	0.82	0.14–2.66
Bladder and kidney (188–189)				
– male	1	2.95	0.34	0.02–1.67
– female	0	1.17	–	–
Lymphatic and haematopoietic tissue (200–208)				
– male	5	1.56	3.21	1.17–7.10
– female	2	1.28	1.56	0.26–5.16
All cancer sites				
– male	24	27.77	0.86	0.55–1.28
– female	21	22.13	0.95	0.59–1.45

* standardized incidence ratio ** 95% confidence interval

incidence ratio, compared with the crude incidence rate, reflects the age structure of the population on Pellworm: 21% of the island inhibitants are 65 years and older, whereas only 15% in Saarland are in that age group.

Table II shows the standardized incidence ratios for all cancer sites. With the exception of neoplasms of the lymphatic and haematopoietic system in men none of the differences was statistically significant. All four men with leukaemia/ lymphoma and the 17-year-old boy with an acute lymphoid leukaemia had been living on Pellworm from birth or more than 15 years. We could not detect any exceptional features with regard to their occupation or living conditions which would explain this difference. In 1991, all persons with cancer who were still living were tested for the HTLV-virus type I – all with negative results.

Some cancer sites (respiratory organs/female or melanoma/female) seem markedly increased with standardized incidence ratios of 1.9 or 2.9. However, these rates result from only one or two cases during seven years – with the bias of distorted statistical proportions if standardized ratios are calculated. The extremely broad confidence intervals, including 1.0, reveal that the increased rates might be random.

Discussion

An important index for the quality of a cancer registry is a low rate of cases confirmed by death certificate only (DCO). All except three cases reported in this study could be verified by histology or cytology. Patients with cancer might have gone to the mainland for diagnosis and treatment and, therefore, not be included in the registry. However, all death certificates on the island were issued by UK or his partner and nearly all inhibitants were seen at the surgery at least once within recent years. Thus, an unrecognized outmigration of patients with cancer and consecutive underreporting of new episodes of cancers can be excluded. The registration rate of nearly 100% and a DCO-rate of 0% provided a highly valid basis for our study. Compared with other cancer registries, this high "diagnostic intensity" might contribute to a somewhat higher incidence rate.

The prima vista impression of an increased cancer incidence rate on the island of Pellworm could not be confirmed. The erroneous impression was the result of the age structure of the population, which showed a marked peak for people over 65 years. On average, the incidence rate was even a bit lower than that in the Saarland registry, probably due to urban-rural differences in cancer rates (2–4). This tendency was not statistically significant.

Only one result is outstanding: the significant excess of leukaemia and lymphoma in men, all of them living more than fifteen years on the island before the diagnosis was established. Several risk factors for the onset of cancer of the lymphatic and haematopoetic system are controversially discussed:

For adults an association between non-Hodgkin's lymphoma and the HTLV-virus type I has been suggested (9, 10). Cattle leukaemia is one possible trigger for this virus (11). But for more than ten years no cattle leukaemia has been reported on Pellworm, and none of the six patients was tested positive for HTLV-I. Some studies reported a significantly increased risk of developing (dying from) leukaemia and lymphoma in farmers (12, 13). For non-Hodgkin's lymphoma there is a proven association with occupational activities when phenoxyherbicides have been used for prolonged periods (14–16). Thus, use of pesticides may be a possible factor in the increased rate of leukaemia/lymphoma on Pellworm since many inhibitants are working in agriculture.

Janerich et al (17) found higher incidence rates for both cancers in those areas of west New York State that had been exposed to a flood disaster. Besides biochemical causes the authors suggest psychophysical stressors as aetiological factors. There may be an association between the occurrence of many humid areas on Pellworm and the rise of cancer. Some recent studies discussed the possible influence of population mixing: a significant increase of childhood leukaemia and non-Hodgkin's lymphoma in some rural areas that received a large influx of external workers might be an indication for an infection underlying leukaemia (18, 19). There is a growing influx of tourists into the isolated population of Pellworm, but any association with the excess of leukaemia/lymphoma for the adult population must remain speculative.

Overall, it is impossible to interpret the increased rate of one cancer site by a descriptive study. It could, however, provide a hypothesis for an analytical, case-control study which includes individual data about place of residence, occupation, and lifestyle factors. Hole & Lamont (20) express scepticism about small area analyses in cancer epidemiology. They discuss the danger that random variation alone can produce substantial differences in observed rates between small areas (21). Although our reference, the Saarland registry, is a valid registry of a sufficiently large area, the possibility of random excess for leukaemia and lymphoma in men on Pellworm due to multiple testing should be cautiously considered. Moreover, a possible bias due to the definition of age classes for standardization must be kept in mind. Since the people of Pellworm are generally older than the people of the Saarland, the mean age in the highest age group might be higher on Pellworm, resulting in standardized incidence rates that are generally biased towards high values (to an unknown extent).

For small area analyses, Hole & Lamont (20) recommend *a priori* hypotheses and research periods of more than ten years. Following their arguments, we should not attach too much importance to the high rate of lymphoma and leukaemia that was found. A new observation study on the island of Pellworm should be restricted to one *a priori* hypothesis (increased rate of cancer of the lymphatic and haematopoietic tissue).

More generally, however, this approach demonstrates the feasibility of a general practice-based research to examine the perception of an increased proportion of cancer in the catchment area of the practice. Provided that the rate of patient registration in the area under investigation can be determined and that nearly all death certificates are issued by a clear-cut number of doctors, general practice is suitable for cancer registry and will produce excellent low DCO-rates. Other important incidence or prevalence data may be provided as well. This does not imply that primary care data will replace cancer registries which co-ordinate the acquisition of data from a variety of sources, but data from general practices could be used in the absence of cancer registries.

And what about Theodor Storm's literary dictum of cancer as a prominent disease of the marshland? At least for Pellworm we could show that this observation was probably caused by the predominence of old people on this island. According to our study, no other pecularity of the marshlands could be held responsible for inducing cancer. But the wisdom of our ancestors might be in Storm's novel and our study should not, for all time, exclude such coincidences.

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